In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 12-155V

Filed: November 2, 2021

NICOLE MATTEN *as parent and legal Representative of the Estate of her Daughter, KM*	*	PUBLISHED
Petitioner,	*	Ruling on Entitlement; Influenza ("Flu") Vaccine; Parainfluenza Virus Type 1, Hypersensitivity; Eosinophilic Myocarditis; Death
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Patricia Finn, Esq., Patricia Finn, P.C., Nanuet, NY, for petitioner.
Jamica Littles, Esq., U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

Roth, Special Master:

On March 6, 2012, Nicole Matten ("Ms. Matten" or "petitioner") filed a petition on behalf of her minor child, K.M., pursuant to the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10 *et seq.*[2] ("Vaccine Act" or "the Program"). Petitioner alleges that K.M. died as a result of the influenza ("flu") vaccine she received on December 2, 2011. *See* Petition, ECF No. 1.

Petitioner alleges that the flu vaccine K.M. received at her seven-year-old well child visit caused K.M. to develop headache, fever, lethargy, vomiting, confusion, body aches, and difficulty breathing as a result of a hypersensitivity reaction, which ultimately led to eosinophilic and/or hypersensitivity myocarditis, arrythmia, cardiac arrest, and K.M.'s death on the morning of December 6, 2011.

[1] This Ruling has been designated "to be published," which means I am directing it to be posted on the Court of Federal Claims' website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (codified as amended at 44 U.S.C. § 3501 note (2006)). **This means the Ruling will be available to anyone with access to the internet.** However, the parties may object to the Ruling's inclusion of certain kinds of confidential information. Specifically, each party has fourteen days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole Ruling will be available to the public. *Id.*

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (1986). Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

Respondent initially argued that K.M. had a parainfluenza virus type 1 infection that caused lymphocytic myocarditis resulting in her death; the flu vaccine played no role in her death. At hearing, however, respondent argued that K.M. had a parainfluenza virus type I infection that caused a deadly bacterial pneumonia and sepsis resulting in her death and the influenza vaccine played no role in K.M.'s death.

Upon review of the evidence submitted in this case, the undersigned finds that petitioner is entitled to compensation under the Vaccine Act. Petitioner has satisfied her burden of showing by preponderant evidence that the flu vaccination administered to K.M. on December 2, 2011 was a substantial factor in causing her death. Respondent has failed to provide sufficient evidence of an alternative cause. The case shall accordingly proceed to damages.

I. PROCEDURAL HISTORY

Ms. Matten filed her petition on March 6, 2012. ECF No. 1. On March 12, 2012, petitioner filed medical records along with a Statement of Completion. ECF Nos. 5, 6. Following assignment to Special Master Golkiewicz, petitioner filed additional medical records and a Declaration of No Additional Records on April 12, 2012. ECF Nos. 9, 10.

On May 22, 2011, this matter was reassigned to then Chief Special Master Patricia Campbell-Smith. ECF No. 11. Respondent filed a Rule 4(c) Report on May 31, 2012, stating based "[on] the existing record, petitioner has failed to provide preponderant evidence in support of her petition for compensation," and therefore "the petition must be dismissed." Resp. Rpt. at 7, ECF No. 12.

Petitioner filed additional medical records and a Statement of Completion on September 24, 2012. ECF Nos. 15, 16. The matter was then reassigned to Special Master Dorsey on January 14, 2013. ECF No. 20.

Following three extensions of time within which to file an expert report, petitioner filed an expert report from pediatrician Dr. Lawrence Palevsky on June 10, 2013. Pet. Ex. 8, ECF No. 25. Petitioner filed medical literature and the curriculum vitae of Dr. Palevsky on June 14, 2013. ECF Nos. 26-29.

On September 6, 2013, petitioner filed K.M.'s autopsy report. Pet. Ex. 10, ECF No. 35.

Following various motions filed by petitioner addressing expert's rates, extensions of time to file additional information, and extensions of time in which to file a supplemental expert report, petitioner filed the expert report of Dr. Anthony Chang, a pediatric cardiologist, along with accompanying medical literature and Dr. Chang's CV on May 5, 2014. Pet. Ex. 11-13, ECF Nos. 66, 67.

On August 21, 2014, respondent filed expert reports from Dr. Sara Vargas and Dr. James Perry. Resp. Ex. A, ECF No. 70; Resp. Ex. P, ECF No. 72. Petitioner then filed expert reports from Dr. Chang and Dr. Laurel Waters. Pet. Ex. 14, ECF No. 76; Pet. Ex. 15, ECF No. 85; Pet. Ex. 16, ECF No. 86.

The matter was reassigned to the undersigned on October 21, 2015. ECF No. 93.

On April 29, 2016, the matter was set for a two-day entitlement hearing, March 20-21, 2017. Pre-Hearing Order, ECF. No. 104.

However, nine months after the hearing was set, on January 23, 2017, a status conference was held following petitioner's Motion for an Extension of Time within which to file her pre-hearing submission. Motion, ECF No. 112; Scheduling Order, ECF No. 113. Petitioner submitted that review of her file revealed the records to be incomplete because records and counsel's computers had been destroyed in Hurricane Sandy in October of 2012. Petitioner asked that the hearing be adjourned for ninety days in order to secure the missing records and provide copies to her experts. Further, she added her experts' opinions may change following receipt of the complete records. It was unclear at the time what records were missing and whether petitioner's counsel was referencing records she previously had or records she never had. Respondent's attorney objected to any adjournment and suggested the parties move forward as scheduled but leave the record open for additional proceedings if necessary. Petitioner was ordered to file a Status report by February 7, 2017, advising which records were missing and how the missing records would negatively impact her experts if the matter was to proceed as scheduled. *See* Scheduling Order, ECF No. 113.

Another conference was held on February 15, 2017, following the filing of affidavits from petitioner's experts, which referenced the previously missing records having been received by them on January 25, 2017. The records were filed with the Court on February 7, 2017. *See* Affidavit of Dr. Waters, ECF No. 116; Affidavit of Dr. Chang, ECF No. 118; Pet. Ex. 43. The newly filed records were the same as the records filed as Pet. Ex. 1, with the addition of handwritten notes of the pediatrician documenting the events in the emergency room on the morning of December 6, 2011. Pet. Ex. 43.

During the February 15, 2017 conference, petitioner's counsel again asked for an adjournment of the March 2017 hearing due to the destruction of her records and computer in Hurricane Sandy in 2012. Respondent objected, submitting that all the records claimed to have been destroyed were filed into CM/ECF on or before September 24, 2012 and were therefore accessible. The age of the case was raised, and petitioner's counsel alluded to delays in the matter being caused by the Court. The docket revealed otherwise, with petitioner having filed ten motions for extension of time during the pendency of this case for a total of 401 days, and her current request for an adjournment of a hearing that had been scheduled nearly a year earlier. *See generally* ECF Nos. 19, 21, 23, 40, 48, 62, 64, 77, 83, and 114.

Petitioner's counsel then advised she was unsatisfied with the opinions of her experts. At this time, it became evident that petitioner's case was not adequately prepared for hearing. I adjourned the hearing so the case could be properly prepared. Deadlines were set for supplemental expert reports for both parties and the hearing was rescheduled for April 30 and May 1, 2018. Scheduling Order, ECF No. 119.

Subsequent delays in this case were partially at the hands of respondent. On the morning of April 30, 2018, as the entitlement hearing was set to begin, respondent's counsel advised on the record that respondent's expert, Dr. Vargas, contacted her the day before, on April 29, 2018, to advise she was amending her opinion on the cause of death. Respondent's counsel advised that she

had immediately telephoned petitioner's counsel to inform her of same. Tr. 5-9. Petitioner's counsel moved to bar Dr. Vargas's opinions, and after a detailed record was made by both counsel, counsel agreed that Dr. Vargas would testify first. Petitioner then would be provided whatever time was necessary for her experts to address Dr. Vargas's amended opinions. Tr. 10-29.

The hearing proceeded on April 30, 2018 and May 1, 2018, with Dr. Vargas and Dr. Perry testifying for respondent and Dr. Chang testifying for petitioner. Dr. Waters, petitioner's pathologist, provided some preliminary testimony, but her opinions were reserved for a later date so she could address Dr. Vargas's amended opinions on the cause of death. *See* Tr. 24-30.

At the conclusion of the hearing on May 1, 2018, petitioner's counsel renewed her motion to bar Dr. Vargas arguing that petitioner was prejudiced by Dr. Vargas's current opinion on the cause of K.M.'s death. I advised petitioner's counsel that I was giving her six months for her experts to evaluate and respond to the amended opinions of Dr. Vargas. Dr. Vargas was also being ordered to provide a comprehensive supplemental written report detailing her current opinion along with all the literature relied on. Therefore, any prejudice that potentially existed would be alleviated by the time a decision was issued in this matter. Tr. 327-34.

An Order issued on May 2, 2018 for the filing of demonstrative exhibits DE-9 and DE-10, produced for the first time at hearing, by May 16, 2018; Dr. Vargas's supplemental report detailing her opinions by June 15, 2018, a date the doctor agreed to; and Dr. Waters supplemental report in response to Dr. Vargas's opinions by August 14, 2018. The hearing was set to continue on October 22, 2018 and October 23, 2018. ECF No. 140.

On May 21, 2018, respondent filed a Motion seeking a 30-day extension for the filing of Dr. Vargas's report. ECF No. 145. An extension to July 16, 2018 was granted. ECF No. 146.

Dr. Vargas's supplemental expert report was filed on July 16, 2018 and designated as Resp. Ex. II. ECF No. 147. The literature relied on by Dr. Vargas was filed on July 17, 2018 and July 18, 2018. ECF Nos. 148-149. Following two motions for extension of time, both granted, petitioner filed her responsive report from Dr. Waters on October 5, 2018. Pet. Ex. 47.

Prior to continuing the hearing, the matter was assigned to Special Master Oler for Alternative Dispute Resolution. ECF No. 152. On October 9, 2018 the matter was removed from ADR. ECF No. 156.

The hearing resumed as scheduled on October 22, 2018 and October 23, 2018.

After the hearing concluded, additional literature referenced during the hearing was ordered for filing. Also discussed was Dr. Shapiro's autopsy file, which contained email exchanges and communications between Dr. Shapiro, the medical examiner who performed the autopsy on K.M., and individuals at the CDC after Dr. Shapiro sent the autopsy slides to the CDC noting his suspicions of a hypersensitivity reaction and the flu vaccine's involvement in K.M.'s death. Petitioner's counsel requested 45 days to consider deposing Dr. Shapiro. A joint status report was ordered to be filed by December 7, 2018. ECF No. 162.

Petitioner filed literature and a Joint Status Report on December 7, 2018, advising that Dr. Shapiro agreed to be deposed in Vermont on May 15, 2019. ECF No. 169. Dr. Shapiro was deposed on May 15, 2019. ECF No. 171. The transcript of the deposition was filed into the record on June 14, 2019. ECF No. 172.

Dr. Shapiro's file was thereafter filed into the record by petitioner, and on August 16, 2019, respondent advised by way of Status Report that the record was complete. *See* ECF Nos. 174, 176.

The parties filed a joint status report on September 23, 2019 advising that they did not wish to file post hearing briefs. ECF No. 177. The record was closed on that date. ECF No. 178.

The matter is now ripe for entitlement decision.

II. SCIENTIFIC TERMS

Lymphocytes[3] are mononuclear nonphagocytic leukocytes[4] that are the body's immunologically competent cells and their precursors. There are various types of lymphocytes such as B cells, which produce antibodies and secrete cytokines,[5] and T cells, which are activated by antigens and directly or indirectly cause cell death. **Neutrophils**[6] are mature granular leukocytes with properties of chemotaxis,[7] adherence to immune complexes, and phagocytosis.[8] **Eosinophils**[9] are granular leukocytes that also participate in combatting parasites and infections.

Myocarditis refers to heart muscle inflammation caused by direct external antigen exposure such as viruses, bacteria, parasites, and drugs or to autoimmune activation against self-antigens. Pet. Ex. 37 at 1.[10] Children with myocarditis generally present with acute or fulminant disease, and pediatric myocarditis is most commonly caused by viral etiology. Myocarditis is a well-known cause of sudden and unexpected death, with the incidence of lethal myocarditis in sudden pediatric deaths ranging from 9% to 17%. Resp. Ex. CC at 1;[11] Pet. Ex. 22 at 2.[12] The diagnosis of myocarditis requires inflammatory cell infiltrate with myocyte necrosis.[13] Pet. Ex. 22 at 2.

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[3] *Dorland's Illustrated Medical Dictionary* 1070 (33rd ed. 2019) [hereinafter "*Dorland's*"].
[4] Leukocytes are more commonly known as white blood cells.
[5] Cytokines are "a generic term for non-antibody proteins released by one cell population (e.g., primed T lymphocytes) on contact with specific antigen, which act as intercellular mediators, as in the generation of an immune response." *Dorland's* 460.
[6] *Dorland's* 1255.
[7] Chemotaxis is "directional movement of a cell or organism in response to a chemical concentration gradient." *Dorland's* 336.
[8] Phagocytosis is "endocytosis (or ingestion by another cell) of particulate material such as microorganisms or cell fragments…the engulfed material is killed and digested." *Dorland's* 1402.
[9] *Dorland's 622.*
[10] Jacques Rizkallah et al., *Eosinophilic Myocarditis: Two Case Report and Review of the Literature*, 6 BMC RSCH. NOTES 538 (2013), filed as "Pet. Ex. 37."
[11] Catherine Allan & David Fulton, *Clinical Manifestations and Diagnosis of Myocarditis in Children*, available in www.uptodate.com (last visited Jan. 13, 2016), filed as "Resp. Ex. CC."
[12] Roger W. Byard, *Sudden Death in the Young*, CAMBRIDGE UNIV. PRESS 181-82 (2010), filed as "Pet. Ex. 22."
[13] Myocytes are muscle cells and necrosis is the sum of changes indicative of cell death caused by enzymatic degradation. *Dorland's* 1205; *Id.* at 1218. Myocyte necrosis is specified, in addition to inflammation, because there is a normal population of lymphocytes within the myocardium; Roger, *supra* note 12.

Lymphocytic and/or viral myocarditis usually contains infiltrates that are lymphocytic but may be neutrophilic. Resp. Ex. CC at 4; Resp. Ex. I at 2.[14] Eosinophils are not a feature of viral myocarditis. Pet. Ex. 34 at 6.[15] Well established causes of viral myocarditis in children are enterovirus, coxsackie B, adenovirus, influenza, parvovirus B19, cytomegalovirus, and poliomyelitis. Resp. Ex. I at 2; Resp. Ex. CC at 1. Clinical myocarditis related to parainfluenza virus type 3 has been reported. Children with viral myocarditis present with a history of recent respiratory or, less frequently, gastrointestinal illness within two weeks prior to presentation and with fever, myalgia, and malaise several days prior to the onset of heart dysfunction symptoms. Resp. Ex. CC at 1.

Eosinophilic and/or hypersensitivity myocarditis is characterized by focal or diffuse myocardial inflammation with infiltrating lymphocytes, plasma cells, and eosinophils. It is drug-induced or secondary to parasitic infections of the heart. Pet. Ex. 34 at 4; Resp. Ex. I at 3; Pet. Ex. 36 at 4;[16] Pet. Ex. 8.12 at 1432.[17] Eosinophilic myocarditis is rare in children. Pet. Ex. 37 at 1; Pet. Ex. 35 at 1.[18] Presenting signs of eosinophilic myocarditis include fever, chills, malaise, weight loss, acute coronary syndrome-like features, heart failure, tachy-or brady-type arrhythmias, and sudden death. Pet. Ex. 37 at 3. Hypersensitivity myocarditis is the clinical diagnosis generally associated with eosinophilic myocarditis and is due to allergic reactions caused by hypersensitivity to various agents.[19] Pet. Ex. 34.

Human Parainfluenza Virus[20] commonly cause upper and lower respiratory illnesses within two to seven days after exposure with symptoms which include upper respiratory illness, fever, runny nose, and cough. Pet. Ex. 27 at 2, 6.[21] Lower respiratory illnesses include croup,[22] bronchitis,[23] bronchiolitis,[24] and pneumonia. Other symptoms of parainfluenza infection are ear infection, irritability, and decreased appetite. Pet. Ex. 8.2.[25] There are four types of parainfluenza

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[14] KAMRAN MIRZA & ALIYA HUSAIN, *CHAPTER 8: THE HEART* IN *BIOPSY INTERPRETATION OF PEDIATRIC LESIONS* 254-71 (Jonathan I. Epstein ed., 2014), filed as "Resp. Ex. I."

[15] John J. Fenoglio et al., *Drug Related Myocarditis*, 12 HUMAN PATHOLOGY 900-907 (1981), filed as "Pet. Ex. 34."

[16] Kyoung-Hee Sohn et al., *Eosinophilic Myocarditis: Case Series and Literature Review*, 5 ASIA PACIFIC ALLERGY 123127 (2015), filed as "Pet. Ex. 36."

[17] Embiya Dilber et al., *Acute Myocarditis Associated With Tetanus Vaccination*, 78 MAYO CLINIC PROC., LETTERS TO THE EDITOR 1431-33 (2003), filed as "Pet. Ex. 8.12."

[18] Henry F. Krous et al., *Sudden Death in a Neonate with Idiopathic Eosinophilic Endomyocarditis*, 8 PEDIATRIC & DEVELOPMENTAL PATHOLOGY 587-92 (2005), filed as "Pet. Ex. 35."

[19] *Hypersensitivity myocarditis, Dorland's Medical Dictionary Online,* https://www.dorlandsonline.com/dorland/definition?id=91286&searchterm=hypersensitivity+myocarditis (last visited Oct. 14, 2021).

[20] Despite the name, human parainfluenza viruses are not the same as influenza viruses.

[21] Kelly Henrickson, *Parainfluenza Viruses*, 16 CLINICAL MICROBIOLOGY REV. 242-264 (2003), filed as "Pet. Ex. 27."

[22] Croup is the condition resulting from acute partial obstruction of the upper airway; characteristics include resonant barking cough, hoarseness, and persistent stridor. *Dorland's* at 430.

[23] Bronchitis is inflammation of bronchi, which are the large air passages between the windpipe and bronchioles in the lungs. *Dorland's* at 249, 250.

[24] Bronchiolitis is the inflammation of the bronchioles, which are the smallest air passages in the lungs, and usually occurs in children less than two years old. *Dorland's* at 248.

[25] National Center for Immunization and Respiratory Diseases, *Human Parainfluenza Viruses (HPIVs)*, CTRS. FOR DISEASE CONTROL & PREVENTION (Nov. 5, 2012), https://www.cdc.gov/parainfluenza/about/symptoms.html, filed as "Pet. Ex. 8.2."

viruses that cause upper and lower respiratory illness in children. Approximately five million lower respiratory tract infections occur each year in children under the age of five, one-third of those are parainfluenza type 1. Resp. Ex. H at 1;[26] Resp. Ex. K.[27] Parainfluenza virus types 1, 2 and 3 are second only to respiratory syncytial virus ("RSV") for acute respiratory infections among children younger than age 5. Resp. Ex. H at 1. Parainfluenza virus infections are common community acquired respiratory illnesses, with most children between six and ten years of age having experienced mild or asymptomatic primary infections. Immunity is incomplete and infections occur throughout life. Pet. Ex. 27 at 6.

Pneumonia[28] is inflammation of the lungs with consolidation; the alveolar air spaces fill with cellular debris, inflammatory cells, and insoluble proteins. It can be caused by viruses, fungi, or bacteria. **Bacterial pneumonia** is caused by bacteria infecting the lungs; it can occur on its own or develop after another illness. Bacterial pneumonia can cause patchy consolidation, bronchopneumonia,[29] or involve an entire lobe of the lung, lobar pneumonia,[30] or both patterns can overlap. Bronchopneumonia is often multilobed and bilateral. Resp. Ex. LL at 1.[31] Histologically, bacterial bronchopneumonia has inflammation consisting of neutrophils that fill the bronchi, bronchioles and alveoli. *Id*. Bacterial pneumonia usually represents as an extension of a pre-existing bronchitis or bronchiolitis and tends to occur more in infancy and old age. Resp. Ex. KK at 1.[32] A medical examiner will often see bronchopneumonia secondary to another disease process, and sudden deaths due to primary pneumonia are uncommon. *See* Resp, Ex. MM at 1.[33] "Occasionally, [a medical examiner] will see a young child with a vague history of some respiratory symptoms over a couple of days, interpreted as being nothing but a cold by the parents. These children are often found to have patchy bronchopneumonia involving all lobes or bronchiolitis." *Id*.

Polymerase Chain Reaction ("PCR") is an amplification of viral DNA and is the most helpful testing in detecting viral genomes.[34] Resp. Ex. CC at 4. PCR testing can detect and distinguish RSV, influenza A, influenza B, and the four types of parainfluenza viruses which cause the majority of viral lower respiratory infections in children and are a significant cause of disease

[26] Wen-Kuan Liu et al., *Epidemiology and Clinical Presentation of the Four Human Parainfluenza Virus Types,* 13 BMC INFECTIOUS DISEASES 28 (2013).
[27] Maria Terlizzi et al., *Quantitative RT Real Time PCR and Indirect Immunofluorescence for the Detection of Human Parainfluenza Virus 1, 2, 3,* 160 J. VIROLOGICAL METHODS 172-77 (2009).
[28] *See Dorland's* at 1450-1452; *Stedmans Medical Dictionary* at 703310.
[29] Bronchopneumonia is an acute bacterial pneumonia with inflammation of the walls of the smaller bronchial tubes, with varying amounts of pulmonary consolidation due to spread of the inflammation into peribronchiolar alveoli and the alveolar ducts. *Stedmans Medical Dictionary* at 124780.
[30] Lobar pneumonia is a type of acute bacterial pneumonia with abundant edema, usually limited to just one lobe of a lung. *Dorland's* at 1451.
[31] BURTON & SINGER, PEDIATRIC NATURE DEATH IN FORENSIC PATHOLOGY OF INFANCY AND CHILDHOOD 870 (Collins KA & Byard RW eds., 2014), filed as "Resp. Ex. LL."
[32] Though not submitted for this statement, this article notes that in clinically diagnosed or suspected pneumonia, it is important to review the clinical record, in particular, imaging and laboratory studies. Resp. Ex. KK at 1.
[33] DIMAIO & DIMAIO, FORENSIC PATHOLOGY 77 (2001), accessed via googlebooks.com, Oct. 11, 2018, filed as "Resp. Ex. MM."
[34] A viral genome is the entirety of the genetic information encoded by the nucleotide sequence of a virus; it is DNA or RNA in viruses. *Dorland's* at 762.

in immunocompromised patients. Pet. Ex. 29 at 5.[35] PCR testing has been used to detect viral genome in inflamed myocardial tissue. Resp. Ex. I at 2. PCR analysis for viral genomes is available for nine viruses identified in causing myocarditis: adenovirus, cytomegalovirus, EBV, enterovirus, Human herpes virus 6, influenza A, Parvovirus, RSV, Hep C. Resp. Ex. D at 5.[36]

III. MEDICAL & FACTUAL RECORD

A. K.M.'s Health Prior Receiving the Flu Vaccine

K.M. was born on September 9, 2004 in Newport, R.I. Pet. Ex. 6 at 10. There is no dispute that K.M. had no prior medical conditions that contributed to her death. She received all her childhood vaccines without event. Pet. Ex. 1 at 5-6.

B. K.M.'s Health During and Post-Vaccination

On Friday, December 2, 2011 at 10:30 a.m., K.M. was presented to Dr. Moseley, her pediatrician, for her seven-year-old well child visit. K.M. was in the first grade, rode a bike with a helmet, was a Girl Scout, watched TV, played video games, played with her friends and siblings, and cleaned her room. Pet. Ex. 1 at 60-61; Pet. Ex. 43 at 4. She lived with her parents and siblings, ate well and engaged in family meals. She had no allergies and took no medications. Pet. Ex. 1 at 62-63; Pet. Ex. 43 at 5. Physical examination on that day was normal, her ears were clear there was no rhinorrhea, no mouth lesions, no tonsillar hypertrophy, her neck was supple with no thyromegaly[37] and no regional adenopathy[38] of the lymph nodes. There was no heart murmur, lungs were clear to P&A,[39] the abdomen was soft with normal bowel sounds and no tenderness, she had full range of motion of all joints, no cyanosis, clubbing or edema of the extremities, and she was neurologically within normal limits. She had no rashes. Pet. Ex. 1 at 65-66; Pet. Ex. 43 at 7. Hemoglobin was done and normal at 16.1, urinalysis was normal, hearing and vision screening were normal. Pet. Ex. 1 at 67, 74; Pet. Ex. 43 at 8. An influenza vaccine was given in K.M.'s left arm. Pet. Ex. 1 at 5-6, 66; Pet. Ex. 43 at 7.

On Sunday evening, December 4, 2011, K.M.'s mother telephoned Dr. Moseley's office at 8:18 p.m. to report that K.M. had a bad headache, vomiting, and a fever of 102.3F despite taking Tylenol. Pet. Ex. 1 at 20.

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[35] Kate E. Templeton et al., *Rapid and Sensitive Method Using Multiplex Rel-Time PCR for Diagnosis of Infections by Influenza A and Influenza B Viruses, Respiratory Synctial Virus, and Parainfluenza Viruses 1, 2, 3, and 4*, 42 J. CLINICAL MICROBIOLOGY 1564-69 (2004), filed as "Pet. Ex. 29."

[36] Resp. Ex. D

[37] Thyromegaly is another term for goiter, which is an "enlargement of the thyroid gland, causing a swelling in the front part of the neck." *Dorland's* at 787, 1896.

[38] Adenopathy is another term for lymphadenopathy, which is a "disease of the lymph nodes, usually with swelling." *Dorland's* 1069. Regional lymphadenopathy is "disease and swelling of most or all of the lymph nodes in an area, usually secondary to an infection or cancer in the swollen area." *Id*.

[39] P&A is "percussion and auscultation," which is "the act of striking a part with short, sharp glows as an aid in diagnosing the condition of the underlying parts by the sound obtained," *Dorland's* at 1389, and "the act of listening for sound within the body, chiefly for ascertaining the condition of the lungs," *Dorland's* at 177, respectively.

On Tuesday morning, December 6, 2011 at 8:45 a.m., petitioner telephoned Dr. Moseley's office advising K.M. needed to be seen and a 10:30 a.m. appointment was scheduled. Moments later petitioner called back to report that K.M. looked blue. She was told to bring K.M. in immediately. K.M. arrived at the pediatrician's office at approximately 9:23 a.m., carried by her mother. The receptionist immediately summoned the physicians and nurses. Dr. Bannach noted fixed dilated pupils, with no audible heart rate or pulses. CPR was started. EMS arrived and transported K.M, Dr. Moseley, and Dr. Bannach to the emergency room at North Country while Dr. Bannach and Dr. Moseley continued CPR in the ambulance. No heart rate was achieved in the pre-hospital phase. Pet. Ex. 1 at 70; Pet. Ex. 43 at 11; Pet. Ex. 5 at 1-2.

The ER record documented a 9:38 a.m. arrival in cardiac arrest from Newport Pediatrics with CPR in process. The emergency room physicians and staff along with Drs. Moseley and Bannach worked to save K.M. A chest x-ray for tube positioning showed no pleural fluid, no pulmonary parenchymal abnormality,[40] or other gross abnormalities. Pet. Ex. 43 at 32. White blood count was normal, but red blood count, hemoglobin, hematocrit, and platelet counts were low. *Id.* 27. K.M.'s dad advised K.M. had received a flu shot on Friday, there were no ingestions, no narcotics, or benzodiazepines in the house accessible to K.M, and she had respiratory symptoms over the weekend. Following a half hour of cardiopulmonary resuscitation and multiple doses of epinephrine there was a return of heartbeat and carotid pulse, though no palpable femoral pulse. Arterial blood gas remained low with prognosis for length of code, poor. Arrangements for transfer to Dartmouth Hospital were made. However, K.M.'s condition then deteriorated and she was pronounced dead at 10:35 a.m. *Id*. at 13, 20, 38-39. The assessment was sudden cardiopulmonary arrest of unknown etiology. *Id*. at 14.

a. Affidavit of Petitioner, Nicole Matten, K.M.'s Mother

Petitioner submitted an affidavit but did not testify at hearing.[41] Pet. Ex. 44.

Petitioner took K.M.to the pediatrician on December 2, 2011 for her seven-year-old well child physical. Dr. Moseley examined her and said she was healthy with no concerns. K.M. received a flu vaccine in her left arm. Pet. Ex. 44 at 1.

The following day, December 3, 2011, the family went to Burlington, about two hours from home. That afternoon, K.M. complained she was tired and had a headache, so they headed home arriving around 7:00 in the evening. K.M. was given Tylenol and went to bed. Pet. Ex. 44 at 1.

Petitioner affirmed the following morning, around 9 a.m. on December 4, 2011, K.M. again complained of a headache and was given Tylenol. The family went to Mr. Matten's Christmas party for work. At the party, K.M. did some arts and crafts, went on a hayride, and received a gift from Santa. The family then went to get their Christmas tree. They arrived home around 2:00 p.m. and K.M. again complained of a headache. Petitioner gave her another dose of Tylenol. K.M. decorated ornaments with her family, but she did not seem interested and continued to complain

[40] Pulmonary parenchymal refers to the essential or functional elements of the lung. *See Dorland's* at 1363, 1529.
[41] I advised counsel it was not necessary for Ms. Matten to be present or testify at hearing; the decision was hers to make. Petitioner chose not to testify at or attend the hearing.

that her head hurt. Around 4:30 p.m., she fell asleep for an hour and awoke complaining that her head still hurt. She had a temperature of 102.3 and began vomiting. Petitioner called the pediatrician. Pet. Ex. 44 at 1-2.

According to petitioner, the pediatrician on call was not from her pediatric practice. She was told to alternate Tylenol and ibuprofen every three hours, make sure K.M. drank fluids and to keep an eye on her through the night. Pet. Ex. 44 at 2. At around 7:00 p.m. that evening, K.M. complained to her dad that her head and body hurt. She continued to vomit and complain of headache and body aches through the night. *Id*.

Petitioner affirmed that on Monday, December 5, 2011, K.M. still had a fever, was lethargic, and stated, "Mommy, I feel like I don't now (sic) where I am," which petitioner assumed was caused by the fever. K.M. slept most of the day only getting up for about 15 minutes to color with her little sister, then went back to sleep on the couch. Pet. Ex. 44 at 2.

Petitioner recalled the night of December 5, 2011 into the morning of December 6, 2011, K.M. "was up and down all night," and slept only one to two hours at time. She would awake crying that her body and head still hurt "really bad" and she continued to throw up. She cried most of the night and could not get comfortable. Petitioner rubbed her body, trying to make her comfortable and take away the pain, but nothing worked. Pet. Ex. 44 at 2. At around 7:30 a.m. on the morning of December 6, 2011, K.M. complained she was cold. Petitioner cuddled her to warm her, both falling asleep until about 8:30 a.m. when petitioner awoke and noted K.M's hands and legs were "blotchy purple". Petitioner called the doctor and was given a 10 a.m. appointment. While dressing K.M, petitioner noted that the area around her lips was turning purple and called the doctor's office that she was bringing K.M.in now. *Id*. at 2-3.

According to petitioner, the doctors' office was about 20 miles from home. She held K.M.in her lap in the back seat of the car. K.M. stopped breathing on the way. When they arrived, petitioner carried K.M. into the doctor's office, she felt unusually heavy. Petitioner yelled, "Help! She isn't breathing" to the receptionist, who called the doctors and nurses. Pet. Ex. 44 at 3.

Petitioner affirmed K.M. was taken from her, and the doctors and nurses began to work on K.M. A nurse jumped up on the gurney to do chest compressions. She was told K.M. was not breathing, they were transferring her next door to the hospital, and the doctors were going with her. The doctors and nurses in the emergency room tried to resuscitate K.M. They called a helicopter to transfer her to Dartmouth Hitchcock, but the weather was too bad to fly so petitioner was told K.M. would be transferred by special ambulance. Within seconds, petitioner was told that there was nothing more that could be done. K.M. was pronounced deceased at 10:35 a.m. Pet. Ex. 44 at 3.

C. The Autopsy Report of Dr. Steven Shapiro, Chief Medical Examiner of the State of Vermont

An initial autopsy report contained the following: "Myocarditis of unknown etiology"; well seven-year-old female child examined on December 2, 2011; Influenza vaccination, left arm on December 2, 2011; Onset of headache, fever (102.3), vomiting 12/4/11 (anamnestic); treated with

Tylenol and Motrin; complaints of body aches and dyspnea 12/6/11 around 9:30; status post emergent resuscitation. Findings included: myocarditis, tracheobronchitis,[42] hepatic triaditis,[43] reactive lymphoid changes in the spleen, thymus and bowel, visceral congestion,[44] and hypoxic-ischemic encephalopathy.[45] Pet. Ex. 4 at 1. Significantly, there was acute neuronal necrosis characterized by cytoplasmic hypereosinophilia in the hippocampus. *Id*.

The autopsy findings further included inflammatory mononuclear cells[46] in multiple sections of the heart. Lymphocytes were rare; there were scattered eosinophils and neutrophils. There were also regions of scattered red blood cell extravasation.[47] Lung sections over microscopic anatomy was maintained. There was intravascular congestion and focal artifactual atelectasis.[48] Air spaces were mostly clear although there were rare areas of proteinaceous edema fluid. In the submucosa of the airways, there were moderately dense inflammatory infiltrates, seen in the bronchioles, bronchi, trachea, and larynx. The infiltrates were mostly lymphocytic although eosinophils were easily found. There was infiltration in the esophagus and stomach, which was mostly lymphocytic but also contained eosinophils, and moderate dense inflammatory infiltrates in the liver, which were mostly mononuclear and eosinophils were common. There were reactive changes in the spleen and thymus and dense inflammatory infiltrates seen in the sections of the ileum and cecum, also reactive. Pet. Ex. 11 at 10.

Dr. Bundock, a neuropathologist, conducted a review of the brain slides at Dr. Shapiro's request. His findings included acute neuronal necrosis characterized by cytoplasmic hypereosinophilia and loss of nuclear detail in the hippocampus, diffuse acute neuronal necrosis, inflammation, viral inclusion, and microglial nodules in the frontal lobe/meninges; acute neuronal necrosis in the parietal cortex and white matter; and acute necrotic changes in the cerebellum. Her diagnosis was hypoxic-ischemic encephalopathy. Pet. Ex. 11 at 10.

Dr. Shapiro filed a VAERS report on December 8, 2011. Pet. Ex. 7.

Dr. Shapiro then filed a revision to the Death Certificate and concluded: "Myocarditis of unknown etiology days following seasonal influenza vaccination with concurrent Parainfluenza virus type 1 infection." Pet. Ex. 3.

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[42] Tracheobronchitis is inflammation of the trachea and bronchi. *Dorland's* at 1915.
[43] Hepatic triaditis is inflammation of the hepatic triad, which is the grouping of the tributaries of the hepatic artery, veins, and bile duct at the angles of the lobules of the liver. *See Dorland's* at 1929.
[44] Visceral congestion is excessive or abnormal accumulation of fluid in any large interior organs of the body. *See Dorland's* 399, 2037.
[45] Hypoxic-ischemic encephalopathy is encephalopathy resulting from asphyxia. In infants presumed to have suffered prenatal or perinatal asphyxia, common symptoms are lethargy, feeding difficulties, and convulsions; serious cases may involve necrosis of neurons in the brain with psychomotor retardation and spastic motor deficits such as cerebral palsy. *Dorland's* at. 608.
[46] Inflammatory mononuclear cells are cells that only have one nucleus; a term used especially in reference to phagocytic cells such as macrophages. *Stedmans Medical Dictionary* at 559060.
[47] Extravasation is discharge or escaped of blood or some other fluid normally found in a vessel or tube, into the surrounding tissues. *Dorland's* at 657.
[48] Atelectasis is the "decrease of loss of air in all or part of the lung, with resulting loss of lung volume itself." *Stedmans Medical Dictionary* at 82320.

On December 13, 2011, Dr. Shapiro wrote to Dr. Sherif Zaki at the CDC about a seven-year-old well child who received a flu vaccine and became ill with flu like symptoms, developed difficulty breathing and died. "Postmortem cultures of lung, spinal fluid and blood were negative for bacteria. Lung was also negative for virus although a nasopharyngeal swab detected Parainfluenza type 1 by PCR." Pet. Ex. 11. at 26. Dr. Shapiro detailed his histological finding and forwarded paraffin blocks of the lung, liver, spleen, and heart to Dr. Zaki requesting help regarding the possible etiology of findings. *See id*.

Dr. Shapiro was included in communication on January 4, 2012 between Dr. Elaine Miller, CDC, and Dr. Kelso, epidemiologist for Infectious Disease at the Vermont Health Department, which documented the testing being conducted at the CDC. PCR analysis of extracts of the combination of tissues was positive for parainfluenza type 1 and negative for influenza A and B, enterovirus, and RSV. PCR for influenza on blocked tissue including upper airway and lung were negative. Immunohistochemistry for enterovirus on heart tissue was negative. Attempts at viral isolation were underway. The email stated, "We cannot rule out the role of vaccine in the death; however, the absence of influenza by PCR and no significant eosinophils or other evidence of hypersensitivity would not make it likely. The most significant finding is the myocarditis in conjunction with upper airway inflammation which we will pursue further." Pet. Ex. 11 at 14-16.

On January 19, 2012, Dr. Shapiro issued a Final Report of Autopsy which included all his findings from the initial autopsy report along with the conclusions of the CDC:

> Conducting airways and lung: tracheobronchitis, bronchiolitis and mild interstitial pneumonitis. Heart: multifocal acute myocarditis. Liver: minimal portal inflammation. There was molecular evidence of type 1 parainfluenza virus infection and no immunohistochemical evidence of type 1, 2 or 3 parainfluenza virus infection; no molecular evidence of influenza type A (including H1N1) or B infection, respiratory syncytial virus (RSV) infection or parechovirus infection and no immunohistochemical or molecular evidence of enterovirus infection. The CDC conclusion was Heart and lung positivity for parainfluenza virus type 1. Cause of Death: Myocarditis of unknown etiology days following seasonal influenza vaccination with concurrent Parainfluenza virus type 1infection.

See. Pet. Ex. 11 at 5-6.

In email exchanges on February 27, 2012 between Dr. Shapiro and Dr. Ritter, CDC, Dr. Ritter asked if Dr. Shapiro was planning to write up this case as there was some interest at the CDC due to the paraflu-associated myocarditis aspect. Pet. Ex. 11 at 17. Dr. Shapiro responded he thought that too but also thought "[t]he eos[sinophilis] in the liver, lungs and bowel as well as the heart, suggest some type of systemic response." *Id*. Though he agreed myocarditis was the "lethal mechanism" of death, he did not agree on the underlying cause of the myocarditis. "[M]y thoughts are this kid had a revved up immune system, possibly from the Parainfluenza, then got the vaccination, designed to give an immune response, and she developed some type of systemic hypersensitivity resulting in the myocarditis and other findings. Hard to prove, but I think blaming the death 100% on a Parainfluenza virus is equally harder to prove, which is why I worded the D[eath] C[ertificate] so." *Id*.

In an email dated March 6, 2012, Dr. Ritter advised Dr. Shapiro that she had looked at additional slides he had sent and agreed the eosinophils were definitively "impressive in the GI sections!" She advised of her intent to review them with other pathologists on histopathology rounds the following day. Pet. Ex. 11. at 19. No further communications were filed.

IV. EXPERTS

A. Petitioner's Experts

a. Lawrence Palevsky, M.D.

Dr. Palevsky is a board-certified pediatrician and a diplomate of the American Board of Integrative Holistic Medicine. Since 2005, he has operated his own practice, Holistic Child Health, at Northport Wellness Center in New York. Pet. Ex. 9. Dr. Palevsky is a member of the Medical Advisory Board for the National Vaccine Information Center. *See Fresco v. Sec'y of Health & Human Servs.*, No. 06-469, 2013 WL 364723 at *17 (Fed. Cl. Spec. Mstr. Jan. 7, 2013) (noting the content on the website suggests that the National Vaccine Information Center is an anti-vaccine organization).

b. Laurel Waters, M.D.

Dr. Waters is board certified in pediatric pathology, nuclear medicine, and anatomic and clinical pathology. She was offered as an expert in pathology, and respondent's counsel agreed. Tr. 353. On cross, Dr. Waters explained that she is an assistant clinical professor at the UC Davis School of Medicine, Department of Pathology and Laboratory Medicine, as a volunteer and has always been a volunteer. Her work is pro bono. Tr. 392-94. Dr. Waters spends 20% of her time at UC Davis or preparing for presentations at UC Davis, generally the second and fourth Tuesday of each month. Tr. 394-396. She cannot sign pathology reports, has no hospital privileges, and has not trained students on microscope in quite some time. She was involved but withdrew from a pediatric pathology fellowship in 1999.[49] Tr. 397-98. She has been in part-time positions since approximately 2000. She could not recall the last time she performed an autopsy. Tr. 400-01. In 2012-2013 she was a full-time medical director in the employment development department of a disability insurance branch; this did not include work as a pathologist. She handled workplace health issues for 13,000 employees statewide and educated physicians on disability ICD-9 diagnoses, disability insurance, paid family leave, and SDI. Tr. 401-02. She has only published abstracts and is not an academic physician. Tr. 403-04.

Dr. Waters was offered and accepted as an expert in pathology.[50] Tr. 353.

c. Anthony Chang, M.D.

Dr. Chang is a pediatric cardiologist and chief intelligence and innovation officer at Children's Hospital of Orange County. He is the medical director of the Heart Failure Program at

[49] Her exchange was rather contradictory about this and her inclusion of the fellowship on her CV. Tr. 399.
[50] Respondent however questioned Dr. Waters on her experience and CV. *See* Tr. 392-405.

the hospital and the founding president of the Pediatric Cardiac Intensive Care Society, which focuses on critically ill children with heart disease. He has edited a textbook, now in its second edition, on heart failure in children and young adults. His areas of expertise include cardiac intensive care and acute illnesses in the ICU setting, including myocarditis. Tr. 126. Dr. Chang received his undergraduate degree at Johns Hopkins University, his medical degree at Georgetown University, completed his pediatric residency at Children's National Medical Center and his cardiology fellowship at Children's Hospital and University of Pennsylvania. Tr. 128.

Dr. Chang was offered and accepted as an expert in pediatric cardiology. Tr. 128.

B. Respondent's Experts

a. Sara Vargas, M.D.

Dr. Vargas is a pathologist who received her undergraduate degree at Harvard University and her medical degree at University of Vermont. She did an extra year as a student fellow in pathology, her residency in pathology, with one year of lung pathology, at Brigham & Women's Hospital in Boston, and a fellowship subspecializing in pediatric pathology at Boston Children's Hospital in 1998 and 1999. Tr. 30-31. Thereafter, she stayed on staff at Boston Children's Hospital doing anatomic pathology, and a smaller percentage of time at Brigham & Women's Hospital doing lung pathology. Tr. 31. Dr. Vargas covers the autopsy service at Boston Children's Hospital about one week out of every four. Tr. 32. She defines herself as a lung pathology specialist, spending about 20 percent of her time with lung specimens. Tr. 290, 326-27. Dr. Vargas teaches residents and fellows at Brigham & Women's Hospital, lectures at conferences and writes papers on unusual cases. Tr. 33. She also has a teaching appointment at Harvard Medical School. She has done original research and written 87 peer reviewed publications. She does research primarily in pediatric pathology or lung pathology and performs peer reviews on journals. She is the assistant editor of the main pediatric pathology journal, Pediatric and Developmental Pathology. Tr. 35. She was associate editor of the 2018 textbook, Practical Imaging: Evaluation of Infants and Children. Tr. 36. In June of 2018, she received an award for distinguished academic achievement from her medical school. Tr. 37; Resp. Ex. B-1.

Dr. Vargas was offered and accepted as an expert in pathology. Tr. 38.

b. James Perry, M.D.

Dr. Perry is a pediatric cardiologist who went to Princeton University then University of Rochester for medical school. He spent three months at Massachusetts General in intensive care and three months in London at Great Ormond Street in cardiology and intensive care. He completed internships and residency in pediatrics at Children's Hospital in Philadelphia and his fellowship in 1986 at Texas Children's Hospital, Baylor College of Medicine in Houston in cardiology and electrophysiology. He worked at Children's Hospital in San Diego from 1993 until 2004, when he went to Yale as chief of pediatric cardiology and professor of pediatric cardiology. He went to Children's Health-Heart Center Group in Minneapolis for a short time and returned to San Diego in 2009. He is currently a professor of pediatrics and director of electrophysiology care at University of California-San Diego, now Rady Children's Hospital, with an appointment as

professor in bioengineering. He also holds a consultant appointment at Kapiolani Children's Hospital in Honolulu. In his capacity as professor of bioengineering, Dr. Perry does clinical work with doctoral and post-doctoral students, seeing patients in the clinic and doing rounds in the intensive care unit. Tr. 171-74. Dr. Perry estimates that he has seen 40-50,000 patients over time and performed over 4-5,000 catheter intervention procedures in patients with all kinds of heart disease, primarily arrhythmia, pacemaker, heart failure and intensive care patients. Tr. 174. He has treated over 100 children with myocarditis, not including post-transplant patients. Tr. 175-76. He is board-certified in pediatric cardiology and adult congenital heart disease, and he is certified in arrhythmia and pacemaker care by the International Heart Rhythm Board. Tr. 176. He has conducted research and authored peer reviewed publications and textbook chapters focused on arrhythmias, their causes, and sudden death. Tr. 177-78.

Dr. Perry was offered and accepted as an expert in pediatric cardiology. Tr. 182-187.

C. Petitioner's Expert's Opinions

There was some debate amongst the experts over whether K.M. suffered from a parainfluenza virus type 1 at the time of her death. However, both the CDC and Dr. Shapiro confirmed that parainfluenza virus type 1 was present. Therefore, the portions of the experts' reports and testimony that debate the presence of parainfluenza virus type 1 are not included herein though were considered.

a. Dr. Palevsky's Report

Dr. Palevsky submitted a report but did not testify at hearing. Pet. Ex. 8.

Dr. Palevsky opined that K.M. received an influenza vaccination on December 2, 2011, developed myocarditis, and died on December 6, 2011, "as a consequence of a severe adverse response to this vaccine." Pet. Ex. 8 at 1. More specifically, in the days following her influenza vaccination, K.M. developed respiratory symptoms, vomiting, diarrhea, severe headache, disorientation, thrombocytopenia, acute blood loss, anemia, acute myocardial infarctions, and myocarditis due to a severe adverse chemical hypersensitivity reaction to the flu vaccine.[51] *Id.* at 14.

Dr. Palevsky explained that myocarditis in the pediatric population can be caused by viruses that reach the heart, which include influenza virus, coxsackie virus, parvovirus and adenovirus, bacterial infections such as Lyme disease, or allergic reactions to medications, exposure to certain chemicals in the environment, infections due to fungi or parasites, radiation, diseases that cause inflammation throughout the body, and some drugs. Pet. Ex. 8 at 1.

Dr. Palevsky noted the cause of death as "myocarditis of unknown etiology days following seasonal influenza vaccination, with concurrent Parainfluenza Type 1 infection," with no detection

[51] Dr. Palevsky did not cite to the medical records. Therefore, it is unclear where he found respiratory symptoms, but the evidence in this case does not indicate that K.M. had any significant respiratory symptoms between the time of her vaccination and her death, only headache, fever, nausea, vomiting, body aches, confusion, lethargy, and shortness of breath just prior to her death.

of any virus on lung tissue and blood cultures and pharyngeal culture negative for bacterial infections. Pet. Ex. 8 at 1. In Dr. Palevsky's opinion, the autopsy findings in the upper respiratory system were the result of trauma from resuscitation. Pet. Ex. 8 at 2. Dr. Palevsky added that literature demonstrating an association between the development of myocarditis and a parainfluenza type 1 infection in healthy children does not exist. *Id*. at 3.

Dr. Palevsky opined the influenza vaccine was the cause of K.M.'s death. K.M.'s hemoglobin on Friday, December 2, 2011 was 16.1, but on December 6, 2011, it was 8.9, thrombocytopenic, with a platelet count of 60K, a stark contrast to a mere four days before. Four days after the flu vaccination, K.M. was suddenly anemic either due to acute blood loss or new onset of autoimmune reaction. Bleeding, anemia, and thrombocytopenia are not part of the clinical picture of parainfluenza virus type 1 infection or viral induced myocarditis. Dr. Palevsky opined that the development of thrombocytopenia, anemia due to bleeding, and a probable autoimmune reaction to her own red blood cells led to the onset of vasculitis, myocardial infarct, myocarditis, and ultimately death. Pet. Ex. 8 at 5. He submitted literature to support a theory of myocarditis:

> "hypersensitivity myocarditis is usually a retrospective circumstantial diagnosis that is suspected because of the temporal link between receiving the vaccination or offending agent and onset of symptoms. Pathogenesis is related to a maladaptive immune system that leads to myocardial injury as evidenced by biopsy specimens in cases of myocarditis after smallpox vaccination that have revealed CD3+ T cell infiltrate with prominent degranulating eosinophils."

Pet. Ex. 8 at 6.[52] He referred to the pathology report, "multifocal regions of myocyte necrosis and phagocytosis (evidence of myocardial infarct) . . . a predominance of mononuclear inflammatory cells…with rare lymphocytes and scattered eosinophils and neutrophils," as evidence of myocarditis linked to receiving the influenza vaccine. *Id*. at 6.

However, Dr. Palevsky cited literature that was not necessarily apt or applicable. For example, Dr. Palevsky noted that myocarditis in children due to parainfluenza virus type 1 infection is rare, though there has been a case reported in a 41-year-old adult, citing *Chen et al.*,[53] Pet. Ex. 8.4. The report involved parainfluenza viral myopericarditis, which is different from myocarditis, and was complicated by rhabdomyolysis. *See id*. He also discussed detection of composition change in myocarditis during systemic diseases K.M. did not have, *see* Pet. Ex. 8.7,[54] and cited a study of an elderly man with a two-day history of fever, chills, fatigue, and increasing shortness of breath two weeks after a flu vaccine. *See* Pet. Ex. 8.8.[55] There was no biopsy done and the conclusion was based solely on temporal relationship to the flu vaccine being a possibility for his myocarditis. *See id*.

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[52] Joseph Murphy et al., *Eosinophilic-lymphocytic Myocarditis After Smallpox Vaccination*, 362 LANCET 1378-80 (2003), filed as "Pet. Ex. 8.11."

[53] Jien-Jiun Chen et al., *Myopericarditis Associated with Parainfluenza Virus Type I*, 22 ACTA CARDIOLOGICA SINICA 163-69 (2006), filed as "Pet. Ex. 8.4."

[54] Sophie Mavrogeni, *Myocarditis in Systemic Diseases and the Role of Cardiovascular Magnetic Resonance*, 53 HELLENIC J. CARDIOLOGY 142-47 (2012), filed as "Pet. Ex. 8.7."

[55] Rodney Jarrell et al., *Rare Association: Possible Myocarditis Secondary to Influenza Vaccination*, 97 S. MED. J. S25 (2004), filed as "Pet. Ex. 8.8."

He submitted numerous articles showing that myocarditis has been linked to diphtheria, tetanus and pertussis vaccine, as well as smallpox vaccine by way of hypersensitivity reaction, none of the articles involved the influenza vaccine. Pet. Ex. 8.9;[56] Pet. Ex. 8.10;[57] Pet. Ex. 8.11;[58] Pet. Ex. 8.12;[59] Pet. Ex. 8.13;[60] Pet. Ex. 8.14.[61]

He also submitted Pet. Ex. 8.15, *Lanza*,[62] which discussed platelet reactivity for an inflammatory reaction following influenza A vaccine. The study suggested a pathophysiological link between inflammation and cardiac autonomic regulation, and vaccine related platelet activation and cardiac autonomic dysfunction which may transiently increase the risk of cardiovascular events. *Id.* at 1.

b. Dr. Waters's Reports and Testimony

Dr. Waters generated six reports in this matter and testified at hearing. Pet. Ex. 20; Pet. Ex. 30; Pet. Ex. 41; Pet. Ex. 42; Pet. Ex. 46 and Pet. Ex. 47.

1. Dr. Waters's First Report

In her first report, Dr. Waters opined that K.M. fatally suffered from lymphocytic myocarditis[63] caused by the influenza vaccine precipitating a cellular immune response mirroring an influenza infection. Pet. Ex. 20 at 11. Dr. Waters described myocarditis as an inflammation of the heart muscle with many causes including infections, drugs, hypersensitivity reactions, metabolic disorders, and radiation. Citing *Byard*, she noted that myocarditis accounts for nine to seventeen percent of sudden deaths in K.M.'s pediatric age group, with the cause of death being acute cardiac decompensation or fatal arrhythmia. *Id.*; Pet. Ex. 22 at 2.[64] Histological findings include infiltration by inflammatory cells, and myocyte necrosis which is required for diagnosis. Pet. Ex. 20 at 8; Pet. Ex. 22 at 2. Citing *Lobo*, Dr. Waters noted that fulminant, or sudden, myocarditis accounts for 30-40% of the myocarditis cases, with a 48% mortality rate. Pet. Ex. 20 at 8; Pet. Ex. 23 at 1.[65] Fulminant myocarditis presents with a sudden onset of cardiac symptoms, usually after nonspecific flu like symptoms and rapidly progresses to severe hemodynamic

[56] S. Amsel et al., *Myocarditis After Triple Immunisation*, 61 ARCHIVES DISEASE CHILDHOOD 403-05 (1986), filed as "Pet. Ex. 8.9."
[57] Maria Thanjan et al., *Acute Myopericarditis After Multiple Vaccinations in an Adolescent: Case Report and - Review of the Literature*, 119 PEDIATRICS e1400-03 (2007), filed "Pet. Ex. 8.10."
[58] Murphy, *supra* note 52.
[59] Embiya Dilber et al., *Acute Myocarditis Associated With Tetanus Vaccination*, 78 MAYO CLINIC PROC., LETTERS TO THE EDITOR 1431-33 (2003), filed as "Pet. Ex. 8.12."
[60] Juliette Morgan et al., *Pericarditis, and Dilated Cardiomyopathy after Smallpox Vaccination Among Civilians in the United States, January–October 2003*, 46 CLINICAL INFECTIOUS DISEASES S242-50 (2008), filed as "Pet. Ex. 8.13."
[61] Frank Boccara et al., *Acute Myopericarditis After Diphtheria, Tetanus, and Polio Vaccination*, 120 CHEST 671-72 (2001), filed as "Pet Ex. 8.14."
[62] Gaetano Lanza et al., *Inflammation-related Effects of Adjuvant Influenza A Vaccination on Platelet Activation and Cardiac Autonomic Function*, 269 J. INTERNAL MED. 118-25 (2010), filed as "Pet. Ex. 8.15."
[63] In her following expert report, *see* Pet. Ex. 30, Dr. Waters amended and clarified that the correct term is eosinophilic or hypersensitivity myocarditis, not lymphocytic myocarditis.
[64] Roger W. Byard, *Sudden Death in the Young*, CAMBRIDGE UNIV. PRESS 181-82 (2010), filed as "Pet. Ex. 22."
[65] Maria Lobo et al., *Fulminant Myocarditis Associate with the H1N1 Influenza Virus: Case Report and Literature Review*, 26 REVISTA BRASILEIRA DE TERAPIA INTENSIVA 321-326 (2014).

deterioration with severe heart failure, cardiogenic shock and potentially fatal arrhythmias. Pet. Ex. 23 at 1. Clinical presentation includes fever, cough, runny nose, nausea, vomiting, abdominal pain, and diarrhea accompanied by dyspnea, arrhythmia, syncope, heart failure and cardiogenic shock. *Id.* at 2. The authors in *Lobo* concluded that H1N1 influenza virus should be considered an etiologic agent of myocarditis and features such as seasonality, endemic status, and vaccination coverage should likewise be considered. *Id.* at 5. Taken in conjunction with *Bratincsak*, which also studied the association between H1N1 and fulminant myocarditis in pediatric patients, Dr. Waters asserted that myocarditis is associated with influenza and may also be associated with the influenza vaccine. Pet. Ex. 20 at 9; *See* Pet. Ex. 24 at 1.

Dr. Waters explained that parainfluenza infections are common childhood illnesses with approximately 75% of all young children in the US having parainfluenza type 1 antibodies by the age of five. Pet. Ex. 20 at 9. Parainfluenza viruses are the second most common cause of lower respiratory disease in hospitalized young children and parainfluenza type 1 is a common cause of croup. *Id.* The CDC overview on human parainfluenza viruses cited by Dr. Waters notes that there are no specific treatments, other than treating symptoms, for parainfluenza illnesses. *Id.* at 9; Pet. Ex. 26 at 2-3.[66] Dr. Waters noted that reverse transcriptase polymerase chain reaction ("RT-PCR") is seen as the gold standard in testing for parainfluenza viruses as it shortens the time for diagnosis and increases sensitivity to ten molecules. Pet. Ex. 20 at 9; Pet. Ex. 28 at 1.[67] However, Dr. Waters also cautioned against the ten-molecule sensitivity of RT-PCR in providing diagnoses as ten molecules could be mere residual antigens left behind. She submitted that such problematic features of RT-PCR have not been considered and such could be the case with K.M.'s diagnosis of parainfluenza. Pet. Ex. 20 at 9; *See* Pet. Ex. 29.[68]

In addressing *Althen* Prong I, Dr. Waters proposed cellular immunity as the medical theory casually connecting the vaccination and K.M.'s death. Pet. Ex. 20 at 11. She described cellular immunity as the process in which antigen-specific cytotoxic T-lymphocytes produce apoptosis in cells containing virus or other targets. T-lymphocytes activate macrophages and natural killer cells which have their own chemical methods to destroy pathogens. "All of these cells produce cytokines which are toxic chemicals." *Id.* at 8. Dr. Waters then explained how virus-specific memory T cells (CD8+ and CD4+) are the cellular immunity arm of adaptive immunity initiated by infection or vaccination. *Id.*; Pet. Ex. 21 at 7.[69] Memory T cells, when compared to naïve T cells, can respond to lower amounts of peptide antigen, make a wider array of cytokines, rapidly become cytolytic, and become home to either lymphoid or non-lymphoid compartments. Though they proliferate as rapidly as every two hours, T cell activation requires 48 to 72 hours before they become active in all those areas. Pet. Ex. 20 at 8. A response can be anamnestic when the antigen

[66] National Center for Immunization and Respiratory Dieases, *Parainfluenza Clinical Overview*, CTRS. FOR DISEASE CONTROL & PREVENTION (Nov. 5, 2012), https://www.cdc.gov/parainfluenza/about/index html, filed as "Pet. Ex. 26."

[67] Jose C. Aguilar et al., *Detection and Identification of Human Parainfluenza Viruses 1, 2, 3, and 4 in Clinical Samples of Pediatric Patients by Multiplex Reverse Transcription-PCR*, 38 J. CLINICAL MICROBIOLOGY 1191-95 (2000), filed as "Pet. Ex. 28."

[68] Kate E. Templeton et al., *Rapid and Sensitive Method Using Multiplex Rel-Time PCR for Diagnosis of Infections by Influenza A and Influenza B Viruses, Respiratory Synctial Virus, and Parainfluenza Viruses 1, 2, 3, and 4*, 42 J. CLINICAL MICROBIOLOGY 1564-69 (2004), filed as "Pet. Ex. 29."

[69] Ian J. Amanna and Mark K. Slifka, Contributions of humoral and cellular immunity to vaccine-induced protection in humans, 411 VIROLOGY 206-15 (2011), filed as "Pet. Ex. 21."

has been seen before, causing a more vigorous response. *Id.* She expressed that K.M.'s response to the December 2, 2011 flu vaccine was likely anamnestic as K.M. had received prior flu immunizations before. *Id.* Dr. Waters also suggested that any concomitant exposure to parainfluenza virus type 1 would have further stimulated an already vigorous cellular immune response, "leading to an excess of cytokines magnifying their toxic effects." *Id.* at 8, 11. Dr. Waters opined that the Institute of Medicine has already put forth the theory that the side effect of vaccines can follow the pattern of the complications of a natural infection. *Id.* at 11; *See* Pet. Ex. 25.[70]

For *Althen* Prong II, Dr. Waters opined that both cellular and humoral immune responses occur with vaccines. Cellular immunity is mediated by lymphocytes and lymphocytes were seen diffusely throughout K.M.'s organs. Pet. Ex. 20 at 11. Dr. Waters opined that the 48 to 72 hours T cell activation lag fit with the course of when K.M.'s clinical illness began 48 hours after vaccination. *Id.* K.M. became very sick and died during the subsequent phase of T cells undergoing rapid proliferation. Following the theory of adverse side effects mirroring natural complications of infections as put forth by the Institute of Medicine, Dr. Waters submitted that myocarditis occurs in influenza with stimulated lymphocytes supporting lymphocytic myocarditis as the final cause of death in K.M.'s case. Pet. Ex. 20 at 11.

For *Althen* Prong III, Dr. Waters opined that the time between K.M.'s receipt of the vaccination on December 2, 20211 and death on December 6, 2011 was an appropriate temporal relationship for the flu vaccine to have initiated a cellular immune response resulting in lymphocytic myocarditis. *See* Pet. Ex. 20 at 11. Dr. Waters noted that the flu vaccine was given on December 2, 2011 during a well-child visit to an apparently healthy seven-year-old girl. Two days later, K.M. was showing toxic signs: bad headache, vomiting, and a fever of 102.3 F, which fit the time course of cellular immunity with a 48 to 72 hours lag time. K.M. was reportedly lethargic and confused on the third day post-vaccination as the proliferative, cytotoxic phase had begun. On the morning of the fourth day, or December 6, 2011, she was brought to the pediatrician's office in extremis. Despite extensive efforts to resuscitate her she was pronounced dead at 10:35 that morning. Dr. Waters opined that K.M.'s concomitant parainfluenza virus type 1 infection combined with the cellular immune response to the vaccine overstimulated her cellular immune response. The lymphocytic myocarditis caused by the vaccine-initiated cellular immune response, which mirrored an influenza infection, resulted in K.M.'s death. Pet. Ex. 20 at 11.

2. Dr. Waters's Second Report

In her supplemental report, Dr. Waters's amended her opinion to accurately reflect that K.M. died from eosinophilic myocarditis rather than lymphocytic myocarditis. Pet. Ex. 30 at 1. Dr. Waters described eosinophils as white blood cells that respond to allergy, parasites, and cancer, and explained that eosinophilic myocarditis, also known as hypersensitivity myocarditis, is an allergic process to drugs and other substances. *Id.* at 4-5; Pet. Ex. 34.[71] Eosinophils have surface proteins which bind IgE and trigger the release of their granules. These granules contain chemicals

[70] Institute of Medicine, *Adverse Effects of Vaccines: Evidence and Causality*, NAT'L. ACAD. PRESS, 402-04, 649-53 App. (2012), filed as "Pet. Ex. 25."

[71] John J. Fenoglio et al., *Drug Related Myocarditis*, 12 HUMAN PATHOLOGY 900-907 (1981), filed as "Pet. Ex. 34."

capable of inducing tissue damage such as apoptosis, necrosis, and the production of free radicals. Pet. Ex. 30 at 4; Pet. Ex. 33 at 2.[72]

Dr. Waters noted that eosinophilic myocarditis is most commonly seen in adults, but when seen in the pediatric population, eosinophilic myocarditis can cause sudden death within hours or a few days of insult or onset of symptoms. The diagnosis is often missed and only found on autopsy. Pet. Ex. 30 at 5; Pet. Ex. 35 at 1;[73] Pet. Ex. 36 at 1;[74] ; Pet. Ex. 37 at 4;[75] Pet. Ex. 38 at 1;[76] Pet. Ex. 39 at 5.[77] She described three stages of eosinophilic myocarditis: acute necrotic, thrombotic, and fibrotic. Without early diagnosis, the acute necrotic stage can be rapidly fatal; patients can present with heart failure or arrhythmia. The fibrotic stage is irreversible scarring within the heart with clinical findings of restrictive cardiomyopathy. Histology at this stage shows fibrosis with few eosinophils or other inflammatory cells. Pet. Ex. 30 at 4-5; Pet. Ex 32;[78] Pet. Ex. 33.[79]

Dr. Waters referenced K.M.'s cardiac autopsy slides in revising her diagnosis to eosinophilic myocarditis. The cardiac autopsy slides showed multifocal polymorphous white blood cell infiltrate including eosinophils, polymorphonuclear leukocytes ("PMN's"), plasma cell and lymphocytes. The pattern of inflammation was primarily interstitial with accompanying edema. Inflammatory cells were seen around the muscle fibers and bundles, and white cells were also seen in the perivascular areas. Pet. Ex. 30 at 3. Dr. Waters opined that the cardiac findings indicated eosinophilic myocarditis. *Id*.

Dr. Waters conceded most of the literature supports an association between myocarditis and smallpox vaccine, but submitted that, in the remaining cases studied, influenza accounted for half of the non-smallpox cases. She also noted that tetanus toxoid was included on a number of lists as a cause of myocarditis, especially eosinophilic myocarditis. Pet. Ex. 30 at 2; Pet. Ex. 31 at 4.[80]

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[72] Pierre-Emmanuel Seguela et al., *Eosinophilic Cardiac Disease: Molecular, Clinical, and Imaging Aspects*, 108 ARCHIVES CARDIOVASCULAR DISEASES 258-68 (2015), filed as "Pet. Ex. 33."

[73] Henry F. Krous et al., *Sudden Death in a Neonate with Idiopathic Eosinophilic Endomyocarditis*, 8 PEDIATRIC & DEVELOPMENTAL PATHOLOGY 587-92 (2005), filed as "Pet. Ex. 35."

[74] Kyoung-Hee Sohn et al., *Eosinophilic Myocarditis: Case Series and Literature Review*, 5 ASIA PACIFIC ALLERGY 123127 (2015), filed as "Pet. Ex. 36."

[75] Jacques Rizkallah et al., *Eosinophilic Myocarditis: Two Case Report and Review of the Literature*, 6 BMC RSCH. NOTES 538 (2013), filed as "Pet. Ex. 37."

[76] Houman Rezaizadeh et al., *Acute Eosinophilic Myocarditis: Diagnosis and Treatment*, 12 Acute Cardiac Care 32-36 (2010), filed as "Pet. Ex. 38."

[77] Haiying Li et al, *A Case Report of Eosinophilic Myocarditis and a Review of the Relevant Literature*, 15 BMC CARDIOVASCULAR DISORDERS 15-23 (2015), filed as "Pet. Ex. 39." At the cellular level, the mechanism of eosinophilic myocarditis involves the activation-stimulated eosinophilic degranulation of a number of compounds, eventually leading to eosinophilic myocarditis. *Id*. at 5.

[78] Ilhan Aslan, *Eosiniphilic Myocarditis in an Adolescent: A Case Report and Review of the Literature*, 23 CARDIOLOGY YOUNG 277-83 (2013), filed as "Pet. Ex. 32."

[79] Pierre-Emmanual Seguela, *Eosinophilic Cardiac Disease: Molecular Clinical and Imaging Aspects*, 108 ARCHIVES CARDIOVASCULAR DISEASE 258-68 (2015), filed as "Pet. Ex. 33."

[80] Michelle Barton et al., *Eosinophilic Myocarditis Temporally Associated with Conjugate Meningococcal C and Hepatitis B Vaccines in Children*, 27 PEDIATRIC INFECTIOUS DISEASES J. 831-35 (2008), filed as "Pet. Ex. 31." The finding of eosinophilic infiltrate on myocardial biopsy strongly suggests a hypersensitivity phenomenon as opposed to a lymphocytic infiltrate characteristic of viral etiology.

In defending her opinion that K.M. died from her vaccination or her vaccination in conjunction with parainfluenza virus type 1, Dr. Waters disagreed with Dr. Vargas's argument that K.M. most likely died from parainfluenza virus type 1, noting that Dr. Vargas failed to recognize that 75% of all children in the US have antibodies to parainfluenza infections by age five. Pet. Ex. 30 at 2-3. She further questioned Dr. Vargas's reliance on *Ohara* in associating parainfluenza virus and myocarditis since the subject there was an adult positive for parainfluenza virus type 3 not parainfluenza type 1. *Id.* at 3.

3. Dr. Waters's Third Report

Dr. Waters submitted a third report dated November 10, 2015 in response to the Court's question of whether any further testing could be done on the autopsy slides. Dr. Waters responded in the negative. Pet. Ex. 41.

4. Dr. Waters's Fourth Report

On March 16, 2016, Dr. Waters issued a fourth report defending her amendment to eosinophilic myocarditis. She explained that she had consulted a colleague who specializes in Pediatric Cardiac Pathology, who felt the number of eosinophils present on the slides were adequate for a diagnosis of eosinophilic or hypersensitivity myocarditis, despite the presence of lymphocytes. Pet. Ex. 42 at 1. Citing a pediatric autopsy manual,[81] she submitted that the number of eosinophils necessary for diagnosis of eosinophilic myocarditis is not well defined; only a few would be needed for diagnosis in an autopsy setting, different than what is required in biopsy. *Id.*

Dr. Waters reiterated that there are many causes for eosinophilic myocarditis, including parasites and medications, and eosinophilic myocarditis has been associated with vaccines in a cardiovascular pathology textbook. Pet. Ex. 42 at 2. She also stated that her finding of nine cases involving flu vaccine associated myocarditis was more compelling than Dr. Vargas's finding of one case involving parainfluenza virus type 3 associated myocarditis. *Id; see* Pet. Ex. 31.[82]

5. Dr. Waters's Fifth Report

Dr. Waters submitted a fifth report just prior to the first scheduled hearing in response to petitioner's "updated" medical records. Pet. Ex. 43; *see* Pet. Ex. 46. Dr. Waters addressed a gastric bleed documented in the autopsy record which all the experts herein agreed played no role in K.M.'s death.[83] Pet. Ex. 46 at 1.

Dr. Waters again referenced the autopsy findings of widespread inflammatory response with lymphocytes and eosinophils, noting those findings to be an indicator of allergy or IgE mediated hypersensitivity response. Pet. Ex. 46 at 2. She reiterated her conclusion that the

[81] MARTA COHEN & IRENE SCHEIMBERG, THE PEDIATRIC AND PERINATAL AUTOPSY MANUAL 343 (Cambridge Univ. Press, 1st ed. 2014).
[82] *Ibid.*
[83] All of the experts addressed K.M.'s gastric bleed in supplemental reports and concluded that it played no role in her death; thus, the discussion of the bleed will not be further discussed in this decision.

mechanism of death was K.M.'s flu vaccine resulting in eosinophilic myocarditis which caused an arrythmia as the terminal event. *Id.*

6. Dr. Waters's Sixth Report

Dr. Waters's final report was issued after the first hearing and in response to Dr. Vargas's amended opinion just prior to hearing that bacteria pneumonia and sepsis secondary to parainfluenza virus type 1 was the cause of K.M.'s death. Dr. Waters characterized Dr. Vargas's opinion as an "abrupt change of the immediate cause of death…from the opinion she had held since 2014." Pet. Ex. 47 at 1.

Dr. Waters explained that when bacterial pneumonia causes death, the findings are widespread, not subtle or controversial; multiple areas of alveoli filled with neutrophils are expected. Pet. Ex. 47 at 1. Countering Dr. Vargas's opinion, Dr. Waters submitted that neither the medical examiner nor the multiple pathologists at the CDC diagnosed "a significant bacterial pneumonia" in this case. Pet. Ex. 47 at 1. Her own "re-examination of the microscopic slides did not alter [her] opinions"—the slides showed no acute exudative pneumonia and the fluid within areas of alveoli was consistent with multifocal pulmonary edema from resuscitation efforts. *Id.* at 2. Dr. Waters noted that while clusters of bacteria in the lungs were seen on KM.'s slides, the clusters lacked neutrophils and were post-mortem artifact. *Id.* at 1-2.

Further, Dr. Waters explained that post-mortem lung culture showed "mod[erate] mixed gram-positive growth," and that "mixed" meant there was no significant bacterial infection. Pet. Ex. 47 at 3. In a true bacterial infection, one type of bacteria overgrows the rest.[84] *Id.* at 4. Dr. Waters asserted that the results would not merely be "mixed gram positive," a very general term to indicate a variety of species. *Id.*

Dr. Waters also addressed the "patchy neutrophilic" inflammation within the alveolar spaces accompanied by exudate. Pet. Ex. 47 at 4. The inflammation was "sparse," as noted by Dr. Vargas, and Dr. Waters opined that "sparse" inflammation would not be consistent with a fatal outcome. *Id.* She also noted that diffuse airspace opacity in a post-mortem x-ray 26 hours after death is most likely artifact of internal lividity, blood pooling, and K.M.'s nonspecific symptoms due to myocarditis. *Id.* Dr. Waters opined that K.M.'s mottled purple extremities were due to blood pooling after death, not a sign of bacterial pneumonia; K.M. had stopped breathing on route to the doctor's office and was noted to have lividity with fixed and dilated pupils upon arrival. *Id.*

Though Dr. Waters conceded that pneumonia is a common cause of immediate death for those suffering from respiratory viral infections or other diseases such as cancer, stroke, and chronic illnesses, K.M. was a well child without any chronic diseases. Even if she had parainfluenza virus type 1, a common respiratory infection in young children, she likely had the infection at least once if not more previously. Further, K.M. was asymptomatic and determined to be a well child following full physical examination the day she received her flu vaccination. She had no chronic illness that could be attributed to a deadly pneumonia. Pet. Ex. 47 at 3. Dr. Waters questioned Dr. Vargas's reliance on *Byard*[85] to support the contention that acute bacterial

[84] Dr. Vargas testified similarly, that in a bacterial infection a single species "takes off". Resp. Ex. II.
[85] Byard, *supra* note 64 at 357-358.

pneumonia can cause sudden death with few signs, opining that there was not enough lung abnormality to consider bacterial pneumonia and noted that those who are asymptomatic prior to the moment of collapse or death are frequently chronic alcoholics, not healthy seven-year-old children. *Id.* at 4.[86] Dr. Waters also challenged Dr. Vargas's reliance on *Jung*[87] to support bacterial pneumonia as the cause of death, noting that there is no support in the literature for bacterial pneumonia resulting from parainfluenza virus type 1. *Id.* at 5.

Dr. Waters relied on and affirmed Dr. Shapiro's conclusions on autopsy that myocarditis was the primary mechanism of death. Pet. Ex. 47 at 2. There was no finding of consolidation of the lungs which would be expected in a fatal bacterial pneumonia, and Dr. Shapiro found eosinophils in the heart, respiratory system, stomach, and liver, which is indicative of a systemic allergic reaction. *Id.* Dr. Waters emphasized that seven people at the CDC signed off on a pathology report following review of autopsy slides and none of them noted bacterial pneumonia. *Id.* Other than Dr. Vargas, no other pathologist reviewing these slides found any significant bacterial clusters in the lungs and no bacterial pneumonia was identified. Everyone appreciated myocarditis though the type was disputed. *Id.* at 3.

Dr. Waters maintained her opinion that K.M. died from an allergic reaction to the flu vaccine resulting in eosinophilic myocarditis. Pet. Ex. 47 at 7.

c. Dr. Chang's Reports

Dr. Chang issued three reports. Pet. Ex. 17; Pet. Ex. 19; Pet. Ex. 45.

1. Dr. Chang's First Report

Dr. Chang reviewed the course of K.M.'s vaccination and rapid decline. He noted that she received a flu vaccine on December 2, 2011, experienced a fever of 102.3, headache, and vomiting on December 4, 2011, was lethargic on December 5, 2011, and had body aches and dyspnea on December 6, 2011, which increased to cyanosis around 9 a.m. and resulted in cardiopulmonary arrest at approximately 9:30 a.m. She was pronounced dead at 10:35 a.m. The autopsy findings included generalized inflammation and myocarditis with multifocal regions of myocyte necrosis, phagocytosis, tracheobronchitis/bronchiolitis/pneumonitis, hepatic triaditis and reactive lymphoid changes in multiple organs such as the spleen, thymus and gastrointestinal track. Parainfluenza virus type 1was detected by PCR in a throat swab but not in any other location. Pet. Ex. 17 at 2.

Dr. Chang opined that K.M. "succumbed to acute hypersensitivity myocarditis, an inflammatory condition of the heart muscle, following her vaccination." Pet. Ex. 17 at 2. Dr. Chang provided two likely and non-mutually exclusive scenarios leading to K.M.'s rapid deterioration and death: fulminant myocarditis, a severe subset of acute myocarditis with a rapid decompensation characterized by severe cardiopulmonary failure within a few hours to days; and ventricular tachydysrhythmias, either ventricular tachycardia or ventricular fibrillation, which are

[86] Dr. Waters quoted a "classic Forensic Pathology book": WERNER SPITZ & RUSSELL FISHER, SPITZ AND FISHER'S MEDICOLEGAL INVESTIGATION OF DEATH 112 (Charles C. Thomas, 2nd ed. 1980).
[87] Hwa Jung et al., *Elucidation of Bacterial Pneumonia Causing Pathogens in Patients with Respiratory Viral Infection*, 80 TUBERCULOSIS & RESPIRATORY DISEASES 358-67 (2017), filed as "Resp. Ex. JJ-5."

not infrequent in acute fulminant myocarditis. *Id.* Dr. Chang opined that K.M.'s influenza vaccination was the "sole inciting agent." *Id.* at 3. He noted that K.M. had no bacterial, fungal, or chronic infection or any diseases. He further noted that K.M. did not have any other infections caused by parainfluenza type 1 virus at the time of vaccination, such as croup, nor is parainfluenza type 1 associated with cardiac disease. Viruses associated with myocarditis were not detected in K.M.'s viral studies. *Id.*

In support of his opinion, Dr. Chang cited *Thanjan*, a case report involving post-vaccination acute myopericarditis in a 17-year-old who received DTaP, meningococcal conjugate, and hepatitis A vaccines. Pet. Ex. 17 at 2n.1; *see* Pet. Ex. 18.[88] After viral infection was ruled out, the proposed mechanism of myocardial injury was hypersensitivity reaction. The pathogenesis of myocardial injury was related to a maladaptive immune response involving CD3+ T-cell infiltrate with prominent degranulating eosinophils. *See* Pet. Ex. 18 at 3.

2. Dr. Chang's Second Report

In his second report, Dr. Chang maintained his opinion that K.M. succumbed to acute hypersensitivity myocarditis. Pet. Ex. 19.

He disagreed with Dr. Vargas's reliance on *Romero-Gomez*,[89] noting that the single case report she relied on involved an immunocompromised child with a parainfluenza virus type 3 infection and a prior influenza A/H1N1 infection. Pet. Ex. 19 at 3. He noted that the heart deterioration found in *Romero-Gomez* could have easily been due to the influenza infection, making reliance on the case study unfounded in the K.M.'s case. *Id.* Dr. Chang further submitted that K.M.'s autopsy showed multi-organ inflammation with findings of anemia and thrombocytopenia. These findings, along with her constellation of symptoms after the vaccine, suggest a systemic inflammatory process more consistent with vaccine related hypersensitivity myocarditis. *Id.*

3. Dr. Chang's Third Report

Dr. Chang's third report again concluded that K.M. died from an acute hypersensitivity myocarditis incited by her influenza vaccination. Pet. Ex. 45 at 2, 4. He addressed K.M.'s gastric bleed and found it non-contributory to K.M.'s death. *See id.*

D. Respondent's Expert's Opinions

a. Dr. Vargas's Reports and Testimony

Dr. Vargas issued six expert reports. Resp. Ex. A; Resp. Ex. AA; Resp. Ex. BB; Resp. Ex. DD; Resp. Ex. II; Resp. Ex. W.

[88] Thanjan et al., *supra* note 57. While insightful, this case study involved a benign clinical course over four stages that lasted for weeks prior to onset of actual symptoms.

[89] Maria Romero-Gomez et al., *Myocarditis Caused by Human Parainfluenza Virus in an Immunocompetent Child Initially Associate with 2009 Influenza A (H1N1) Virus*, 49 J. CLINICAL MICROBIOLOGY 2072-73 (2011), filed as "Resp. Ex. J."

From the time of her initial report, filed on August 21, 2014, until the eve of the May 2018 hearing, Dr. Vargas opined that K.M. died from viral myocarditis secondary to parainfluenza virus type 1. Though she initially mentioned bacterial pneumonia as a possible secondary cause, she never developed a theory in the four years leading to the May 2018 hearing. *See* Resp. Ex. A at 7. At the May 2018 hearing, Dr. Vargas began opining that the true cause of death was bacterial pneumonia secondary to parainfluenza virus type 1. *See* Tr. 5-26.

1. Dr. Vargas's First Report

In her initial report, Dr. Vargas concluded that K.M. died of complications from a parainfluenza virus type 1 infection, with "cardiac arrhythmia due to viral myocarditis" as the most likely mechanism of death. Resp. Ex. A at 12.

Dr. Vargas discussed that the autopsy slides of the airways, lung, heart, and liver examined at the CDC Infectious Disease Pathology Branch showed "tracheobronchitis, bronchiolitis, and mild interstitial pneumonitis," "multifocal acute myocarditis," and "minimal portal inflammation." Resp. Ex. A at 3. Bacterial culture of the lung showed "mixed gram-positive growth" with no growth in blood, and lung gram stain showed moderate leukocytes. *Id*. Parainfluenza virus type 1 was found by PCR though immunohistochemical stains were negative for parainfluenza virus and enterovirus. *Id*. at 3-4. Additional testing was negative for influenza A and B, RSV, parechovirus, and enterovirus. *Id*. Dr. Vargas opined that the lymphocytic inflammation in the pulmonary interstitium, intra- and extra- pulmonary airways, peribronchial lymph nodes, and larynx were typical of viral infection. *Id*. at 6. She expressed that K.M. suffered from chronic longstanding disease, "certainly longer than the 4-day duration between her vaccination for influenza and her death," evidenced on autopsy as widespread lymphocytic inflammation, thickening of the tracheobronchial tree, and copious amounts of lymphoid tissue in the gastric system. *Id*. at 7.

Dr. Vargas submitted that parainfluenza virus type 1 is a common cause of myositis[90] in children and the chronic inflammation seen at K.M.'s left arm, where the vaccination was administered, was consistent with myositis. Resp. Ex. A at 6. Dr. Vargas relied on *Romero-Gomez*[91] to support a causal association between parainfluenza virus and myocarditis; though she admitted that the findings involved parainfluenza virus type 3, not type 1. She suggested that testing for parainfluenza virus type 1 is rarely done thus the incidence may be unappreciated. *Id.* Dr. Vargas explained that a subset of patients with parainfluenza virus type 1 have symptoms of fever, vomiting, diarrhea, and seizure, and therefore concluded that the constellation of autopsy findings and high specificity of viral molecular testing of tissue samples supported a parainfluenza virus type 1 infection causing viral or lymphocytic myocarditis as the mechanism of K.M.'s death. *Id*. at 6.

Dr. Vargas briefly proposed an alternative cause of death: sepsis from a bacterial pneumonia superinfection secondary to viral respiratory tract infection. Resp. Ex. A at 7. She noted that superinfections are a "fairly common complication of viral respiratory infection" and that

[90] Myositis is the "inflammation of a voluntary muscle." *Myositis, Dorland's Online Medical Dictionary,* https://www.dorlandsonline.com/dorland/definition?id=32923&searchterm=myositis (last visited Oct. 25, 2021).
[91] *Ibid*.

K.M.'s postmortem lung weight at approximately twice the expected weight is typically seen in the setting of bacterial pneumonia. *Id.* She further noted that there were neutrophils on the postmortem lung samples submitted for Gram stain, which are typical inflammatory cells recruited in bacterial infection. *Id.*

In defending her opinion, Dr. Vargas noted that the Institute of Medicine has not specifically assessed mechanistic evidence regarding an association between influenza vaccine and myocarditis. Resp. Ex. A at 7. Dr. Vargas criticized Dr. Chang's conclusions as based on temporal relationship alone and submitted that he was limited by reviewing only the autopsy report, which lacked adequate detail of chronic inflammatory changes indicative of a much longer course of disease time as seen on the slides. *Id.* at 8. Further, Dr. Vargas criticized Dr. Chang's opinion that parainfluenza virus type 1 cannot be responsible for a more widespread distribution, citing *Tippet* which discussed parainfluenza virus type 1 causing myositis. *Id.*; Resp. Ex. N. [92] She believed that Dr. Chang failed to appreciate the myositis on K.M.'s arm because it was not mentioned in the autopsy report and Dr. Chang did not review the slides. Resp. Ex. A at 8-9.

Dr. Vargas also disagreed with the finding of hypersensitivity myocarditis. According to Dr. Vargas, hypersensitivity myocarditis histologically shows inflammatory infiltrates consisting predominantly of eosinophils. She opined that K.M.'s microscopic slides showed inflammatory infiltrate of lymphocytes with only occasional eosinophils which would be typical of viral infection. Resp. Ex. A at 9; *see* Resp. Ex. I.[93] She further criticized Dr. Chang placing significance on the laboratory findings of anemia and thrombocytopenia since the blood work was done after prolonged circulatory compromise. Resp. Ex. A at 9. She questioned the literature relied upon by Dr. Chang stating that it did not demonstrate influenza vaccine can cause myocarditis. *Id.* at 10.

Dr. Vargas disagreed with Dr. Palevsky's opinions noting that he underappreciated the respiratory tract disease and chronic inflammation found on autopsy, and she found his opinion that the inflammation was caused by intubation as "unusual." Resp. Ex. A at 11. Further, she asserted that Dr. Palevsky underestimated the association between respiratory virus and myocarditis and misquoted the literature. *Id.* Dr. Vargas added anemia, thrombocytopenia, and blood in the stomach were all consequences of prolonged hypoxia/ischemia followed by reperfusion and/or resuscitative trauma, not the findings of an autoimmune reaction as suggested by Dr. Palevsky. *Id.* at 10-11. Finally, Dr. Vargas criticized Dr. Palevsky for not reviewing the slides and for his lack of understanding of the cellular components of hypersensitivity myocarditis. In her opinion, the infiltration of K.M.'s heart was consistent with myocarditis caused by viral infection. *Id.* at 11.

2. Dr. Vargas's Second and Third Reports

[92] Emma Tippet & Ronald Clark, *Benign Acute Childhood Myositis Following Human Parainfluenza Virus Type-1 Infection*, 25 EMERGENCY MED. AUSTRALASIA 248-51 (2013), filed as "Resp. Ex. N."
[93] KAMRAN MIRZA & ALIYA HUSAIN, *CHAPTER 8: THE HEART* IN *BIOPSY INTERPRETATION OF PEDIATRIC LESIONS* 254-71 (Jonathan I. Epstein ed., 2014), filed as "Resp. Ex. I."

Dr. Vargas's second and third expert reports discussed the presence, duration, and testing for parainfluenza virus type 1 in K.M.[94] Resp. Ex. W; Resp. Ex. AA.

3. Dr. Vargas's Fourth and Fifth Reports

In her fourth and fifth reports, Dr. Vargas maintained her first opinion that K.M. died from complications of parainfluenza virus type 1. Resp. Ex. BB at 1; Resp. Ex. DD at 4. She criticized Dr. Waters's "change" from lymphocytic to eosinophilic myocarditis, finding Dr. Waters' "new diagnosis and new proposal about vaccine causality…both incorrect." Resp. Ex. BB at 1. Dr. Vargas asserted that pediatric lymphocytic myocarditis predominantly involves lymphocytes, with interspersed eosinophils. This is in contrast to eosinophilic myocarditis, in which eosinophils are the predominant inflammatory cell. *Id*. at 1-2; Resp. Ex. I.[95] Dr. Vargas reiterated that the autopsy of heart sections showed myocarditis with predominantly lymphocytic infiltrate, with neutrophils and occasional eosinophils - "eosinophils constitute only a very small fraction of the inflammatory cells." *Id*. According to Dr. Vargas, autopsy heart sections with eosinophilic myocarditis should show a preponderance of eosinophils by definition; therefore a "diagnosis of eosinophilic myocarditis is thoroughly inappropriate" in this matter. *Id*. at 3. She opined that none of the literature relied on by Dr. Waters supports the contention that eosinophils need not be present in large numbers for an eosinophilic myocarditis diagnosis or the conclusion that a histologic appearance such as that in K.M. should be construed as eosinophilic myocarditis. *Id*.

Dr. Vargas reiterated that viruses are well-known causes of lymphocytic inflammation and are the cause of most cases of viral myocarditis in children. Resp. Ex. BB at 4; Resp. Ex. CC.[96] She asserted that Dr. Waters' conclusion that the influenza vaccine was equally as likely to be causal finds no support in the Institute of Medicine publication[97] or any of the literature relied upon. *Id*. at 5.

3. Dr. Vargas's Final Report

In her final report dated July 16, 2018, filed after the May 2018 hearing, Dr. Vargas opined that bacterial pneumonia was the cause of K.M.'s death. Resp. Ex. II at 1.

Dr. Vargas submitted her opinion on the cause of K.M.'s death had actually changed "very little." Resp. Ex. II at 1. Initially, she opined that rather than parainfluenza virus leading to myocarditis resulting in death, the parainfluenza virus led to both bacterial pneumonia and myocarditis, with bacterial pneumonia being more likely the immediate cause of death.[98] *Id*. She explained that she did not initially appreciate the pneumonia histologically, so she did not list pneumonia as the favored cause of death and chose myocarditis instead. *Id*. She stated, "[t]his small shift in interpretation actually makes the facts of the case hold together much more

[94] All experts agreed that parainfluenza was present therefore further discussion of parainfluenza testing is unnecessary.
[95] Mirza & Husain, *supra* note 14.
[96] Catherine Allan & David Fulton, *Clinical Manifestations and Diagnosis of Myocarditis in Children*, available in www.uptodate.com (last visited Jan. 13, 2016), filed as "Resp. Ex. CC."
[97] Institute of Medicine, *supra* note 70.
[98] Interestingly, when Dr. Vargas took the stand again on rebuttal in the second hearing, she testified that myocarditis was a red herring and played no role in K.M.'s death

cohesively in terms of the medical understanding of the cause of death. In that way, the impact on the case could be considered large." *Id.* at 3. Now appreciating an acute exudative pneumonia, Dr. Vargas opined that she was quite convinced that pneumonia was the immediate cause of death as features of the case "align[ed] more strongly than ever with a diagnosis of bacterial pneumonia." *Id.* at 1-2.

According to Dr. Vargas, parainfluenza virus type 1 is a respiratory virus that particularly affects the airway mucosa leading to chronic predominantly lymphocytic inflammatory infiltrate. Resp. Ex. II at 2. Normally, small amounts of bacteria can be handled by a healthy airway which propel microscopic particles and mucus away from the lungs through cilia. However, viral infections compromise the airway mucosa, leaving the lungs more vulnerable to bacteria, and are "well known to lead to bacterial pneumonia." *Id.*; Resp. Ex. JJ-16.[99]

Dr. Vargas submitted that her most recent review of the microscopic sections of the lung showed features of bacterial pneumonia: coccus-shaped bacteria and patchy proteinaceous exudate within the alveoli in all sampled sections. Resp. Ex. II at 3. Patchy neutrophilic inflammation was sparse though seen focally in all sampled sections. The alveolar walls were disrupted in areas of exudate, which occurs in necrosis. *Id.* "This constellation of features is convincing for acute bacterial pneumonia…some species of streptococcus produce pneumonia with disease patterns showing a notable prominence of intra-alveolar blood and proteinaceous material chart eristic of rapid progression as seen in K.M.'s lungs. In rapidly progressive necrotizing pneumonias, the number of neutrophils can be relatively sparse, explaining why they can be difficult to find." *Id.* at 3-4; Resp. Ex. JJ-6.[100] Dr. Vargas further cited the character and distribution of the bacteria in the lung to support her finding of fatal bacterial pneumonia. *Id.* at 4. Streptococcus species are virulent in the lung and grow in clusters and often in chains. She submitted that, in addition to clusters, chains were particularly prominent in the bacteria seen in K.M.'s lung slides suspicious for streptococcus species. *Id.* Further, a postmortem chest x-ray showed "diffuse airspace opacity" which occurs in bacterial pneumonia. *Id.* According to Dr. Vargas K.M.'s symptoms were typical of bacterial pneumonia, including some evidence of cough.[101] The time course for bacterial pneumonia can come on over days and cause death within a few days. *Id.* at 5.

Dr. Vargas cited *Jung* to bolster the connection between K.M.'s parainfluenza infection and bacterial pneumonia, noting that "[i]n one study, 17 of 319 children with parainfluenza virus infection developed post-viral bacterial pneumonia as a complication of their viral infection". Resp. Ex. II at 4. In Dr. Vargas's opinion, the autopsy slides show a parainfluenza infectious process over a week old and "easily could be a month old," suggesting K.M. had a chronic respiratory condition well before receiving her vaccination.[102] Resp. Ex. II at 6. Dr. Vargas added

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[99] David Morens et al., *Predominant Role of Bacterial Pneumonia as a Cause of Death in Pandemic Influenza: Implications for Pandemic Influenza Preparedness*, 198 J. INFECTIOUS DISEASES 962-70 (2008), filed as "Resp. Ex. JJ-16."

[100] RICHARD KRADIN & EUGENE MARK, PATHOLOGY OF PULMONARY INFECTION IN DIAGNOSTIC PATHOLOGY OF INFECTIOUS DISEASE, 158 (Richard K. Kradin ed., 2018), filed as "Resp. Ex. JJ-6."

[101] There is no clear evidence of cough or other respiratory distress in K.M.'s record—K.M.'s father mentioned URI once at the ER; neither mom nor Dr. Moseley documented any respiratory symptoms until just short of her death when she had dyspnea.

[102] Dr. Vargas found it surprising that K.M. had no symptoms before December 3, since the chronic inflammation in sections of the larynx and trachea were well marked and well developed.

the heavy spleen on autopsy was further support of viral infection due to expansion of lymphoid. Resp. Ex. II at 6. "[I]t is difficult to rule out the possibility of superimposed superinfection." *Id.* at 4, 6.

In this final report, Dr. Vargas concluded the parainfluenza virus led to necrotizing bacterial pneumonia and sepsis which caused K.M.'s death. Resp. Ex. II at 8. She then opined that myocarditis played no role, submitting that the myocardial changes in context were more likely due to resuscitation rather than true lymphocytic myocarditis. *Id.* at 7. Additionally, the overlap between the length of time K.M. was in cardiorespiratory arrest before resuscitation and the resuscitation efforts with the use of epinephrine and chest compressions collectively caused patchy areas of extravasated blood, interstitial edema, patchy coagulative necrosis, and variable numbers of acute inflammatory cells including neutrophils and eosinophils. "It is important not to mistake areas such as this for significant antemortem disease." *Id.*

b. Dr. Perry's Reports

Dr. Perry issued two expert reports in this matter. Resp. Ex. P; Resp. Ex. HH.

1. Dr. Perry's First Report

Dr. Perry opined that, while a temporal association existed between the influenza vaccine and death four days later, the autopsy indicated a longer duration of sub-clinical illness, predating the vaccination date. This illness resulted in myocarditis, tracheobronchitis, pneumonia and inflammation of other organs. Resp. Ex. P at 3. Dr. Perry also noted that myocarditis can have a subclinical course extending over several days to more than a week and not come to medical attention until myocardial decompensation has occurred. *Id.* Dr. Perry noted that K.M. had previously received five flu vaccinations without event and that the flu vaccine is not a live virus vaccine. *Id.* Instead, respiratory and cardiac inflammation from a viral etiology are actually fairly common clinical associations, and the PCR results supported parainfluenza virus type 1 as "being an active infectious agent responsible for this child's demise." *Id.* He also opined that K.M.'s prior history is irrelevant; the nature of her myocarditis was "clearly lymphocytic, as recognized as the classic finding in viral myocardial inflammation" and not hypersensitivity reaction which results from eosinophilic infiltrate. *Id.*; *see* Resp. Ex. R;[103] Resp. Ex. S.[104]

Though Dr. Perry could not state with certainty whether K.M. suffered respiratory arrest with subsequent cardiac decompensation and ventricular tachyarrhythmia, a cardiac ventricular arrhythmia coinciding with respiratory illness, or myocarditis causing complete atrioventricular block, he concluded that the viral infection was the etiology. Resp. Ex. P at 4. He opined that cardiac arrhythmia with viral myocarditis is not an infrequent event. *Id.*; *see* Resp. Ex. R;[105] Resp.

[103] Paul Vignola et al., *Lymphocytic Myocarditis Presenting as Unexplained Ventricular Arrhythmias: Diagnosis With Endomyocardial Biopsy and Response to Immunosuppression*, 4 J. AM. COLL. CARDIOLOGY 812-19 (1984), filed as "Resp. Ex. R."
[104] Ayelet Shauer et al., *Acute Viral Myocarditis: Current Concepts in Diagnosis and Treatment*, 15 ISRAELI MED. ASS'N J. 180-85 (2013), filed as "Resp. Ex. S."
[105] Vignola et al., *supra* note 103.

Ex. T;[106] Resp. Ex. U;[107] Resp. Ex. V;[108] He also submitted that anemia and thrombocytopenia are common post arrest findings. *Id*.

Dr. Perry submitted that both Drs. Chang and Palevsky were inaccurate on numerous accounts and concluded that K.M. had viral myocarditis and diffuse inflammation from a viral infection, most likely parainfluenza. "Her death was clearly most likely due to Parainfluenza infection and not from any idiosyncratic or other reaction to an influenza vaccine." Resp. Ex. P at 4.

2. Dr. Perry's Second Report

Dr. Perry issued a supplemental report that criticized Dr. Waters' amendment from lymphocytic to eosinophilic myocarditis as unsupported and unwarranted. *See* Resp. Ex. HH at 2-3. Dr. Perry confirmed his opinion that the cause of death was widespread viral illness with myocarditis and cardiovascular collapse, most likely due to parainfluenza virus type 1 infection. *Id*. at 3.

V. LEGAL FRAMEWORK

A. Petitioner's Overall Burden in Vaccine Program Cases

The Vaccine Act provides two avenues for petitioners to receive compensation. First, a petitioner may demonstrate a "Table" injury—i.e., an injury listed on the Vaccine Injury Table that occurred within the provided time period. § 11(c)(1)(C)(i). "In such a case, causation is presumed." *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006); *see* § 13(a)(1)(B). Second, where the alleged injury is not listed on the Vaccine Injury Table, a petitioner may demonstrate an "off-Table" injury, which requires that the petitioner "prove by a preponderance of the evidence that the vaccine at issue caused the injury." *Capizzano*, 440 F.3d at 1320; *see* § 11(c)(1)(C)(ii).

To prove causation, petitioner must satisfy the three-pronged test established in *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires that petitioner show by preponderant evidence that a vaccination K.M. received caused her death "by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id*. at 1278. Together, these prongs must show "that the vaccine was 'not only a but-for cause of the injury but also a substantial factor in bringing about the injury.'" *Stone v. Sec'y of Health & Human Servs.*, 676 F.3d 1373, 1379 (Fed. Cir. 2012) (quoting *Shyface*, 165 F.3d at 1352-53). Causation is determined on a case-by-case basis, with "no hard and fast *per se* scientific or medical rules." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Petitioner is not required to identify "specific

[106] Tadaaki Abe, et al., *Clinical Characteristics and Long-Term Outcome of Acute Myocarditis in Children*, 28 HEART VESSELS 632-38 (2013), filed as "Resp. Ex. T."
[107] Christina Miyake et al., *In-Hospital Arrhythmia Development and Outcomes in Pediatric Patients With Acute Myocarditis*, 113 AM. J. CARDIOLOGY 535-40 (2014), filed as "Resp. Ex. U."
[108] Richard Friedman et al., *Persistence of Ventricular Arrhythmia After Resolution of Occult Myocarditis in Children and Young Adults*, J. AM. COLL. CARDIOLOGY 780-83 (1994), filed as "Resp. Ex. V."

biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

A petitioner need not show that the vaccination was the sole cause, or even the predominant cause, of the alleged injury; her burden for recovery is to show that the vaccination was a "substantial factor" and a "but for" cause of the injury. *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006); *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999).[109] Once a petitioner has proven causation by preponderant evidence, "the burden then shifts to the respondent to show by a preponderance of the evidence that the injury is due to factors unrelated to the administration of the vaccine." *Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013) (citing § 13(a)(1)(B)).

B. Standards Applicable to Significant Aggravation Claim

Though initially contested amongst the experts in their reports, the medical examiner, Dr. Shapiro and the CDC determined that K.M. was positive for parainfluenza virus type 1 infection. As more particularly set forth at length below, the flu vaccine therefore significantly aggravated K.M.'s condition. The *Althen* test is expanded, and the petitioner has additional evidentiary burdens to satisfy as established in *Loving v. Sec'y of Health & Human Servs.,* 86 Fed. Cl. 135, 144 (2009). In *Loving*, the Court of Federal Claims combined the *Althen* test with the test from *Whitecotton v. Sec'y of Health & Human Servs.*, 81 F.3d 1099, 1107 (Fed. Cir. 1996), which related to on-Table significant aggravation cases. The resultant "significant aggravation" test has six components, which require establishing: (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a "significant aggravation" of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation. *Loving*, 86 Fed. Cl. at 144; see also *W.C.*, 704 F.3d at 1357 (holding that "the *Loving* case provides the correct framework for evaluating off-table significant aggravation claims"). In effect, the last three prongs of the *Loving* test correspond to the three *Althen* prongs.

Subsumed within the *Loving* analysis is the requirement to evaluate the likely natural course of an injured party's preexisting disease, in order to determine whether the vaccine made the petitioner worse than he would have been but for the vaccination. *Locane v. Sec'y of Health & Human Servs.*, 685 F.3d 1375, 1381–82 (Fed. Cir. 2012) (upholding special master's determination that petitioner had failed to carry her burden of proof in establishing that her preexisting injury was worsened by the relevant vaccine); *Hennessey v. Sec'y of Health & Human Servs.*, No.

[109] The Vaccine Act also requires a petitioner to show by preponderant evidence that the vaccinee suffered from "residual effects or complications" of the alleged vaccine-related injury for more than six months, died from the administration of the vaccine, or required inpatient hospitalization and surgical intervention as a result of the alleged vaccine-related injury. § 11(c)(1)(D). It is undisputed that this requirement is satisfied in this case.

01190V, 2009 WL 1709053, at *41–42 (Fed. Cl. Spec. Mstr. May 29, 2009), mot. for review denied, 91 Fed. Cl. 126 (2010). Under this analysis, petitioner need only compare his pre- and post- vaccination conditions. Though petitioner need not compare his current condition to the otherwise expected outcome of his condition, he must still demonstrate that his vaccination affected his condition and was a substantial factor in causing his injury. *Sharpe v. Sec'y of Health & Human Servs*., 964 F.3d 1072, 1082 (Fed. Cir. 2020) (citing *Locane*, 685 F.3d 1375). The critical point of examination is thus "whether the change for the worse in [petitioner's] clinical presentation was aggravation or a natural progression" of the underlying condition. *Hennessey,* 2009 WL 1709053, at *42.5 The Federal Circuit has upheld the determinations of special masters that worsening was not demonstrated in connection with establishing a petitioner's overall preponderant burden of proof for a non-Table causation-in-fact claim. See, e.g., *Snyder/Harris v. Sec'y of Health & Human Servs.*, 553 F. App'x 994, 999–1000 (Fed. Cir. 2014); *Locane*, 685 F.3d at 1381–82.6

C. Legal Framework Governing Factual Determinations

The process for making factual determinations in Vaccine Program cases begins with analyzing the medical records, which are required to be filed with the petition. § 11(c)(2). Medical records created contemporaneously with the events they describe are generally presumed to be more trustworthy. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993); *but see Kirby v. Sec'y of Health & Human Servs.*, 993 F.3d 1378, 1382-83 (Fed. Cir. 2021) (clarifying that *Cucuras* does not stand for proposition that medical records are presumptively accurate and complete). Contemporaneous medical records that are clear, consistent, and complete warrant substantial weight "as trustworthy evidence." *Id*. Indeed, "where later testimony conflicts with earlier contemporaneous documents, courts generally give the contemporaneous documentation more weight." *Campbell ex rel. Campbell v. Sec'y of Health & Human Servs.*, 69 Fed. Cl. 775, 779 (2006); *see United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1948). But petitioners can support their claim with oral testimony if it is credible and consistent with the medical records. *See, e.g., Stevenson ex rel. Stevenson v. Sec'y of Health & Human Servs.*, No. 90-2127V, 1994 WL 808592, at *7 (Fed. Cl. Spec. Mstr. June 27, 1994) (crediting the testimony of a fact witness whose "memory was sound" and "recollections were consistent with the other factual evidence"). Of particular importance in matters involving death, a special master shall consider "any diagnosis, conclusion, medical judgement, or autopsy or coroner's report…regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death" *Whitecotton*, 81 F.3d 1099, 1108 (1996). In short, "the record as a whole" must be considered. § 13(a).

Furthermore, establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of his or her claim. *Lampe v. Sec'y of Health & Human Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. "In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Id*. at 590 (citation omitted). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly ex rel. Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1324 (Fed.

Cir. 2010). The *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). And nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder ex rel. Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

Finally, although this decision discusses some but not all the literature in detail, the undersigned reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty ex rel. Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Human Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

VI. ANALYSIS & DISCUSSION

A. K.M.'s Diagnosis or Mechanism of Death

As Federal Circuit precedent establishes, in certain cases it is appropriate to determine the nature of a petitioner's injury before engaging in the *Althen* analysis. *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1346 (Fed. Cir. 2010). "Each prong of the *Althen* test must be decided relative to the injury." Therefore, the diagnosis or mechanism of death must first be determined.

Prior to the first hearing held on April 30 and May 1, 2018, all the experts and Dr. Shapiro agreed that the mechanism of death was myocarditis. Pet. Ex. 8; Pet. Ex. 45; Pet. Ex. 46; Resp. Ex. BB; Resp. Ex. HH. They disagreed on whether the myocarditis was lymphocytic/viral caused by parainfluenza virus type 1, eosinophilic and/or hypersensitivity due to the flu vaccine alone, or eosinophilic and/or hypersensitivity due to a combination of the flu vaccine and parainfluenza virus type 1. Though initially contested, it was generally accepted by the experts at the time of hearing that K.M. had a parainfluenza virus type 1 infection—the extent and ramifications of such an infection were still disagreed upon. *See* Pet. Ex. 8 at 2; *see* Pet. Ex. 45 at 3; *see* Pet. Ex. 42 at 3; *see* Resp. Ex. BB at 1; *see* Resp. Ex. HH at 1.

At the close of the evidence, Drs. Waters, Chang, and Shapiro maintained that the mechanism of death was eosinophilic and/or hypersensitivity myocarditis, and Dr. Perry maintained it was lymphocytic/viral myocarditis caused by a parainfluenza virus type 1

infection.[110] Dr. Vargas's final opinion was that the mechanism of death was bacterial pneumonia and sepsis caused by a parainfluenza virus type 1 infection. She ultimately concluded that myocarditis was "a red herring" and continued to assert that the flu vaccine played no role. Tr. 543.

Therefore, whether K.M. died from bacterial pneumonia and sepsis or a myocarditis must first be determined.

a. Bacterial Pneumonia

1. Dr. Vargas's Diagnosis of Bacterial Pneumonia

According to Dr. Vargas, the day before the hearing was to begin, she picked up "one of the lung slides" while waiting to leave for the airport and "found that there was neutrophilic inflammation," the kind of inflammation that responds to bacteria consistent with the presence of a respiratory infection and resulting bacterial pneumonia. Tr. 60. Dr. Vargas admitted the slide was the same slide she had previously examined in rendering her opinions in this matter but testified that it was not until the day before hearing that she happened to land on the slide with the microscope in just the right way. Tr. 60, 292-93. In explaining how she did not notice neutrophils when previously reviewing the slides, Dr. Vargas stated that "overwhelming bacterial pneumonia," like the one in this case, can be patchy and focal and not seen in every area of the lung slide, so you must "drive around and look" for it. Tr. 62; 64-65; 482; 489, 491; Resp. Ex. KK. "I can understand why others missed it and why I missed it myself at first." Tr. 62, 474-75.

According to Dr. Vargas, when any amount of bacterial pneumonia is seen on autopsy, it must be included as a possible cause of death and considered "in the context of other findings in the case to make a determination." Tr. 490. She opined that K.M.'s case was difficult: the slides were "very busy" and the bacterial pneumonia was "focal," not everywhere. Tr. 491. She noted that the autopsy slides were made after there had been resuscitation, K.M. had been in cardiorespiratory arrest for a long time, the lungs were weakened by decompositional changes, and CPR had forced blood through the lungs. Thus, she initially dismissed bacterial pneumonia as a potential cause as it "can mimic other—other things." Tr. 100-01. However, in reconsidering and explaining her diagnosis, Dr. Vargas stated that neutrophilic response is a vital response and one must be living to produce it; thus, the changes and sparse neutrophilic inflammation cannot be dismissed merely as from decompensation. *See* Tr. 101.

Dr. Vargas opined that K.M. died of "necrotizing bacterial pneumonia," as a complication of parainfluenza virus type 1 infection. Tr. 48; 309. She admitted she did not see the "full spectrum of histologic findings" the first time she examined the slide, but upon review, when considered with varying types of evidence:[111] the gross findings, laboratory findings, post-mortem radiographs, and the clinical setting of K.M.'s symptoms, the findings all point to bacterial

[110] During the hearing, Dr. Perry amended his opinion to include Dr. Vargas's new opinion, emphasizing that K.M. may have "died with bacterial pneumonia" though he continued to maintain that "the parainfluenza virus was the primary etiology that set up everything downstream." Tr. 218, 220.

[111] All the evidence Dr. Vargas cites as having directed her to the new diagnosis of necrotizing bacterial pneumonia was already part of the record from the time of Dr. Vargas's initial report.

pneumonia. Tr. 48-50, 306. Her "other reason" was that "bacterial infection commonly follows a respiratory—a viral infection and that bacterial infection in the lungs is a virulent problem, and extensive bacterial pneumonia is a common cause of death and well known to cause death." Tr. 49-50.

More specifically, Dr. Vargas relied on K.M.'s heavy lung weight, as a hallmark of bacterial pneumonia, with "bacteria of one kind" in all sections. Tr. 51-52, 58-59, 497-98. She did not agree that the heaviness of the lungs was caused by post-mortem pulmonary edema. Tr. 549. Despite acknowledging that all K.M.'s organs were heavy, she stated that "there's no hard and fast, right or wrong weight" of organs and the lung heaviness was her only interest. *See* Tr. 52-55. Pet. Ex. 10 at ECF 7; Resp. Ex. E. She then cited to tissue samples that showed "mixed Gram-positive bacterial organisms," explaining that neutrophils respond to gram-positive cocci bacteria. Tr. 65-67; 71-72; Tr. 495-96; Pet. Ex. 10 at 32. In K.M.'s samples, the cocci were growing in chains, typical of streptococcus infection. Tr. 67. The antemortem blood culture grew a type of gram-positive coccus, indicating a bacterial infection that has gone into the bloodstream. Tr. 496. Dr. Vargas stated that, "vascular engorgement and fluid, sparse neutrophils and abundant bacteria can be seen in the alveoli" in early stages of low bar pneumonia. Tr. 482-83; Resp. Ex. LL.[112] She opined that literature supports patchy bronchopneumonia found in children with only vague cold symptoms causing sudden unexpected death. Tr. 484, 489, 499; Resp. Ex. MM; Resp. Ex. JJ-12; Resp. Ex. JJ-3. She cited *Jung* showing bacterial pneumonia commonly following upper respiratory viral infection and parainfluenza virus[113] and *Morens* looking at deaths during Spanish flu pandemic from a superimposed bacteria. Tr. 499-500; Resp. Ex. JJ-5;[114] Resp. Ex. JJ-16.[115]

Dr. Vargas used photographs of the decisive lung slide to support her opinion. Tr. 84; Resp. DE. A-9; Resp. DE A-10. Dr. Vargas opined that DE A-9 showed evidence of lymphocytic inflammation that fit a history of a virus. Tr. 85-86, 314. She pointed to "clouds of bacteria" and neutrophils, stating "there are convincing neutrophils here and down here" though it only showed part of what was much more bacteria seen on the slide. Tr. 86-87; 315; 317. She conceded that bacteria can continue to grow following death and was not claiming all the bacteria she saw were there before death. However, she reiterated that the distribution of bacteria throughout the lung, in all sections, of the same type, is common in community acquired pneumonia and could not have all grown after death. Tr. 318; 491-492. Dr. Vargas then presented DE A-10 as a higher-powered image of the slide which showed that the bacteria were coccal-shaped, in clusters, and what is expected to be seen in a community-acquired bacterial pneumonia. Tr. 88. "[H]ere I think they're very nicely kind of forming the chains…we never got to have them speciated in the lab, but I really favor a streptococcus organism." Tr. 88. Dr. Vargas admitted the slide was "very busy" and the neutrophils had to be searched for. Tr. 89.

Dr. Vargas believed K.M. had a "fairly long-standing" viral infection ongoing for weeks before developing into a deadly pneumonia. Tr. 96-98; 474-75. She used a photograph of K.M.'s larynx to support parainfluenza virus type 1 as the precipitating illness, pointing to organized lymphoid cell aggregation, or persistent lymphocytic inflammation, around the airways, lung, and

[112] Barton et al., *supra* note 80.
[113] Parainfluenza virus type 3, not parainfluenza virus type 1, was discussed.
[114] Jung et al., *supra* note 87.
[115] Morens et al., *supra* note 99.

larynx. Tr. 97; Resp. DE A-8. However, she admitted that "there are overlaps in the symptoms that occur from a parainfluenza virus infection and a bacterial bronchial pneumonia, and…overlap between symptoms that occur as a result of those and symptoms that occur in sepsis." Tr. 473. Dr. Vargas claimed K.M.'s cough[116] could be from either infection, but vomiting, headache, fever, nausea, body aches, lethargy, confusion, coldness, blotchy purple hands and legs, and eventually obtundation and death would be attributed to the bacterial pneumonia. Tr. 473-74.

When asked about K.M. being deemed a well child at the time of her examination despite having a "long-standing" viral infection, Dr. Vargas suggested that subtle symptoms of illness were overlooked, or she was truly asymptomatic. Tr. 98; 471-72. When asked how K.M.'s blood work taken in the emergency room could be normal if she was septic and dying from a fatal bacterial pneumonia, Dr. Vargas first responded, in "overwhelming sepsis, you can't mount your white blood cell response and your white blood – your white blood cells can go down instead of up. So you can't rely too much on one single test." Tr. 479-82; Pet. Ex. 43 at 22. She suggested that the test is unreliable and is "known for these pitfalls." Tr. 482. She further discredited the normal bloodwork, noting that blood was taken after cardiorespiratory arrest with blood pooling and lividity, thus the cells clump differently making the ratios invalid and because only viruses were tested for. Tr. 95-96. However, Dr. Vargas later testified that the blood work was not normal; the microbiology report showed "gram-positive cocci" that, when speciated, was found to have staphylococcus epidermidis.[117] Tr. 536; Pet. Ex. 43 at 24.

In response to a throat swab for streptococcus virus being negative, Dr. Vargas stated throat swabs are unreliable with a "substantial" false negative rate. Tr. 70-71. She similarly discredited the normal chest x-ray taken in the emergency room with no pneumonia reported, stating clinical and chest x-ray findings lag behind, the quality of the films in emergency situations are not as good as a routine x-ray or CT scan, or could be the fault of "the radiologist's technique." Tr. 63. However, she found the post-mortem x-ray as informative and supportive of pneumonia with widespread abnormalities in the alveolar sac where air would normally be. Tr. 81-82; Pet. Ex. 10.

Dr. Vargas claimed she did not conclude bacterial pneumonia and sepsis as the cause of K.M.'s death until the hearing because she needed to be "exacting," and needed to "see the full range of supporting evidence to make the diagnosis…" Tr. 72-73; 548. She could not recall how many times she looked at the slides but admitted she did not see the neutrophils before now despite having seen "mixed Gram-positive organisms" during her initial review of the matter. Tr. 71-73, 75, 307. She acknowledged the other pathologists who reviewed the slides in this matter did not find bacterial pneumonia and suggested their lack of findings contributed to her delay in reaching the correct diagnosis of bacterial pneumonia. *See* Tr. 62. Dr. Vargas testified to being "100 percent right" in this case; no one else saw the pneumonia because they were focused on other things and were not experts in lung pathology like she is. Tr. 44-45; 293-96; 551.

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[116] As discussed in footnote 83, there is no record of K.M. having a cough.

[117] This finding is likely insignificant as staphylococcus epidermis is "the most common coagulase-negative species inhabiting the skin and mucous membranes; many strains are pathogens or secondary invaders and cause mainly nosocomial diseases, including wound infection" and nosocomial diseases which are those "pertaining to or originating in the hospital." *Staphylococcus Epidermis, Dorland's Medical Dictionary Online,* https://www.dorlandsonline.com/dorland/definition?id=108213&searchterm=Staphylococcus+epidermidis (last visited Oct. 25, 2021); *Nosocomial, Dorland's Medical Dictionary Online,* https://www.dorlandsonline.com/dorland/definition?id=34355&searchterm=nosocomial (last visited Oct. 25, 2021).

2. Drs. Waters's and Chang's Response to a Bacterial Pneumonia Diagnosis

Dr. Chang was confused by Dr. Vargas's opinion of bacterial pneumonia and maintained that the vaccination led to a fulminant myocarditis, which led to cardiac arrest, with pulmonary edema as part of the cardiopulmonary decompensation. Tr. 135; Tr. 129, 138, 140. He pointed out that the chest x-ray in the emergency room was clear from infiltrates in the lungs, which would not support a bacterial pneumonia diagnosis. Tr. 136-37. As both a clinician and intensivist, he found it hard to imagine a child dying from pneumonia that was not discernable on a chest x-ray. Further, if K.M. had pneumonia severe enough to cause death, she would have had obvious signs of respiratory distress at the time of the vaccination. Tr. 135-36. As a pediatric cardiologist, Dr. Chang stated he never saw such a rapid course of bacterial pneumonia as it is usually a slow process. "I think it unheard of to have a child as well-appearing [as K.M.] and then die of bacterial pneumonia a few days later." Tr. 136.

Dr. Chang disagreed with Dr. Vargas's interpretation of K.M.'s heavy lungs. He explained the heaviness resulted from K.M.'s heart not working due to myocarditis, which caused inadequate blood flow out of the heart - "literally the circulation starts to back up into the lungs" creating pulmonary edema or increased water content in the lungs. Tr. 137. Bacterial pneumonia does not mean the lungs are heavier, and heavier lungs does not mean there is bacterial pneumonia. *Id*. "It's far more likely to be directly due to the increased water content in the lungs from the heart failing." *Id*. Further, all her organs were heavy because when the heart fails other organs, the liver, potentially the spleen, and eventually the entire body will retain fluid to reflect the heart not being efficient in maintaining circulation. Dr. Chang also noted that pulmonary edema can lead to shortness of breath and respiratory distress. Tr. 138.

Dr. Waters, like Dr. Chang, disagreed with Dr. Vargas's diagnosis of bacterial pneumonia. She, too, attributed the heaviness of the lungs on autopsy to pulmonary edema. Tr. 356; 380. She agreed there were small foci associated with neutrophils on the lung slide, but, even so, they were small and nothing that could rise to the level of fatality. Tr. 446-47. She expressed that a deadly pneumonia would be widespread and not missed by multiple pathologists reviewing the same slide. Tr. 356; 358-59; 390; 442; Resp. Ex. II. Further, Dr. Waters opined that "mixed Gram-positive" with no growth in the blood argues against bacterial pneumonia which would have grown a single type of bacteria. Tr. 268-73; 443-44; 450-51; Pet. Ex. 47 at 3.

Dr. Waters agreed with Dr. Chang that the post-mortem x-rays taken 24 hours after death did not show pneumonia but rather post-mortem opacification, which is expected, is consistent with death, and is not clinically significant. Tr. 381. Dr. Waters also explained that the x-rays taken in the emergency room, despite being on a portable x-ray, would have shown pneumonia if it were significant enough to cause death. Additionally, the emergency room x-rays were really premortem since it was quite some time since resuscitation had begun and K.M. already showed signs of death. Tr. 382.

Dr. Waters stated the blood work done in the emergency room was in fact normal as documented. If there was a bacterial infection, neutrophils would have been elevated, and if there

was a viral infection, lymphocytes would have been elevated. The fact that the blood tests were normal when K.M. was brought into the emergency room means she had no active viral or bacterial infection at that time. Tr. 433-36; Pet. Ex. 43 at 27. K.M.'s peripheral bloodwork did not support bacterial pneumonia. Tr. 444-46.

Dr. Waters, though hesitantly, agreed K.M. had an active parainfluenza virus type 1 infection as her own findings included lymphocytes within the trachea, bronchi, and bronchioles consistent with tracheobronchitis and bronchiolitis. Tr. 362; 424-27; 436-37; 453; Pet. Ex. 11 at 28. Regardless, Dr. Waters opined that K.M. was a healthy and asymptomatic child on December 2, 2011. To die four days later from bacterial pneumonia secondary to a long-standing parainfluenza infection, K.M. would have had to have been symptomatic. She opined that pneumonia tends to be a disease of the immunocompromised and chronically ill, not of a seven-year-old deemed healthy just a few days prior. Tr. 363-64.

3. Dr. Shapiro's[118] Response to a Bacterial Pneumonia Diagnosis

Dr. Shapiro maintained throughout his deposition that K.M.'s cause of death was "myocarditis of unknown etiology days following a seasonal influenza vaccination with concurrent parainfluenza type 1 infection," not bacterial pneumonia. Shapiro Dep. at 5-6, 20, 22-25. His inclusion of parainfluenza virus type 1 was based on the CDC findings of molecular evidence in multiple tissues. *Id.* at 40-42; Pet. Ex. 11 at 29. In Dr. Shapiro's opinion, K.M. was a healthy child with a parainfluenza virus type 1 infection which activated her immune system. She then received a vaccine designed to stimulate the immune system, an already revved up immune system. "Her terminal mechanism was most likely a cardiac arrhythmia brought on by the myocarditis." *Id.* at 7, 18-19. "The kid died from a hypersensitivity revved up immune system. She had two very clear instigators of revved up immune system. One, the parainfluenza infection; and two, a vaccination. How that worked in her body to create this hypersensitivity and this myocarditis, I do not know that kind of final physiology…" *Id.* at 25-26.

Dr. Shapiro did not know how Dr. Vargas arrived at her opinion—K.M. did not die from bronchopneumonia from bacteria; Dr. Vargas ignored the myocarditis and the vaccine. Shapiro Dep. at 23, 24, 32. He re-reviewed the slides Dr. Vargas relied on in rendering her opinion that K.M. died of bacterial pneumonia. *Id.* at 6; 11-12. He found "some lymphocytic and neutrophilic margination on the lung slide," which he described as terminal perimortem and overgrowth of bacteria. *Id.* at 8. "Perimortem" is a "dead kind state" before resuscitation is stopped. K.M. was resuscitated for hours before they finally stopped and "every once in a while[,] in those kinds of cases," overgrowth of bacteria is seen. *Id.* at 8. Dr. Shapiro added bacterial pneumonia is a common final mechanism for many different causes of death but seen generally in people who are immunocompromised or debilitated in some way. *Id.* at 8-9. He opined that K.M. did not develop a bronchopneumonia out of the blue. *Id.* at 25-27.

Dr. Shapiro agreed children with normal immune systems can develop viral myocarditis and that Gram stains will show neutrophils with gram-positive cocci that supports pneumonia depending on the species of the infection. However, there are a lot of contaminants, so one would

[118] Dr. Shapiro went to medical school with Dr. Vargas and has known her for 30 years. Shapiro Dep. at 12.

want to see a specific infection in the lung with predominant numbers, "[j]ust seeing bacteria neutrophils does not pneumonia make". Shapiro Dep. at 38-39. He agreed bacteria can be patchy, but the Gram stains were postmortem, so they had little meaning to him; it was a matter of where the interaction plays out in the tissue. "Bacteria grow on slides all of the time. Especially in postmortem, perimortem tissue." *Id*. at 35-36. Though there was some margination, K.M. did not have "a rip-roaring bronchopneumonia" which would look the same in infants, children, adults, and geriatrics. *Id*. at 37. Dr. Shapiro stated, prior to death, K.M. developed non-specific symptoms associated with a lot of diseases: difficulty breathing, vomiting, fever, body aches, headache, and lethargy, with hands, legs, and lips turning blue. *Id.* at 22-25, 27; Pet. Ex. 11 at 4. He did not agree that these were symptoms of bacterial pneumonia or sepsis and reiterated several times, "This child did not have bacterial pneumonia." *Id*. at 20, 22, 24.

Much like Drs. Chang and Waters, Dr. Shapiro emphasized that K.M.'s heavy lung weight was a non-specific finding. Shapiro Dep. 48. He testified that when a person dies, the heart starts to fail and fluid backs up into the lungs; thus, heavy lungs at autopsy are a common finding after death. Further, when people are dying and blood pressure drops, part of the resuscitation process is to put fluid in, which contributes heavy congested lungs. He agreed excessive lung weight is not always unimportant but here it was not important especially with the histology not supporting any kind of bronchopneumonia. *Id*.

Dr. Shapiro testified that, as he does with all myocarditis cases, he forwarded the paraffin blocks to Dr. Zaki's lab at the CDC[119] for testing and to characterize which virus it was. Shapiro Dep. at 33, 47. There was no bacterial pneumonia found by the CDC. *Id*. at 14, 16, 19, 39-40. While he agreed that pathologists often disagree, "it does not change the fact that this child did not have bacterial pneumonia, as far as I'm concerned." *Id*. at 24. Further, Dr. Vargas was not the only expert in lung pathology to review this case. Following receipt of Dr. Vargas's report opining that K.M.'s death was due to bacterial pneumonia, Dr. Shapiro presented the slide to Kelly Butner, M.D. at University of Vermont Medical Center, asking her if he missed something and if she saw pneumonia. Dr. Butner knew nothing about the case, examined the slide, and confirmed what was on the slide was "terminal[120] at best." *Id*. at 32-33, 36, 46, 52. He noted that, in addition to Dr. Butner, Dr. Bundock, the neuropathologist in his office, seven CDC scientists, Dr. Waters, Dr. Chang and Dr. Perry all reviewed the slide, and no one found bacterial pneumonia in this case except for Dr. Vargas. To Dr. Shapiro, this was "significant in the sense that I don't believe there's bacterial pneumonia in this child". Shapiro Dep. at 43-45, 53-54.

4. Dr. Perry's Diagnosis and Response to a Bacterial Pneumonia Diagnosis

For the whole of Dr. Perry's direct testimony, he mentioned nothing about bacterial pneumonia and maintained his opinion that K.M. died of lymphocytic myocarditis caused by parainfluenza virus type 1. Tr. 188-89. Then after a brief recess of the hearing, Dr. Perry returned and for the first time stated K.M. died of bacterial pneumonia. Conceding bacterial pneumonia was

[119] Dr. Zaki's Lab at the CDC is the reference lab for viral immunohistochemical studies on paraffin blocks.

[120] Terminal in this situation refers to that which occurs near or during the time of death.

not mentioned in any of his reports, or during his direct testimony, he stated "I haven't been asked the question. If you ask me the question, I'm happy to answer." Tr. 218.

When asked he then responded: "I think she died with bacterial pneumonia." Tr. 218. He further explained, with "the data we have now, I believe the parainfluenza virus was the primary etiology that set up everything downstream." Tr. 220. "Secondary bacterial infections are very, very common in viral chest infections. So the fact that there is now evidence of bacterial superinfection on top of the primary parainfluenza infection …if anything, strengthens…the course of argument that the child had…extensive pulmonary disease that could have caused respiratory arrest, followed by a cardiac tachycardia from the myocarditis." Tr. 221. Dr. Perry stated that bacterial pneumonia did not change his opinion in this case because parainfluenza virus type 1 was the primary etiology for everything that followed. Despite the presence of bacterial pneumonia, Dr. Perry maintained myocarditis as the mechanism of death.

Then, attempting to align his opinion with Dr. Vargas, Dr. Perry stated, "the evidence shows that she clearly had a parainfluenza infection in her lungs, she clearly had parainfluenza in her heart...she has pathologic evidence of a longer standing viral process in her lungs as well, and that again, is a setup for this bacterial infection."[121, 122] Tr. 221-22. He added bacterial pneumonia in young children causes vomiting, they get dehydrated which exacerbates the process. Extensive pulmonary disease with a virus exacerbates the process of risk of arrhythmia. Tr. 222.

Further, Dr. Perry initially stated the pre- and post-mortem x-rays showed a normal heart size and no pulmonary edema, finding no issue relying on the images taken to opine against heart failure. However, he later agreed with Dr. Vargas that pre-mortem x-rays may not show the pulmonary edema, if "blood can't get in there to make an infiltrate visible, it's not going to show up on the x-ray. It may not show up." Tr. 203-05; 231-32.

5. K.M. Did Not Die of Bacterial Pneumonia

A treating physician's opinions are considered "quite probative," and are entitled to some weight. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1326 (Fed. Cir. 2009); *Capizzano*, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting *Althen*, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence since they are created contemporaneously with the treatment of the vaccinee. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). In the same vein, the opinion of a medical examiner is equivalent to that of a treating physician and should be afforded the same consideration. *Nordwall ex rel. Tori v. Sec'y of Health & Human Servs.,* 83 Fed. Cl. 477, 488 (2008) ("An autopsy report by a medical examiner is without question a contemporaneous medical record").

[121] Dr. Perry acknowledged that K.M. was deemed well on December 2, 2011, the day of vaccination and stated if a child appears sick vaccinations should be deferred, though he did not know why that would be; he guessed that they may not mount a response to the vaccine. Tr. 237; 259-61.

[122] Dr. Perry did not provide citation for parainfluenza virus being found on heart tissue.

Here, the evidence does not weigh in favor of bacterial pneumonia and sepsis as the mechanism of death. Though Dr. Vargas is highly credentialed, she was the only one of more than a dozen individuals who reviewed the slides, who found and concluded that K.M. died from necrotizing bacterial pneumonia and sepsis. Drs. Waters, Chang, Shapiro, and Butner agreed the findings on the lung slide were typical postmortem and/or terminal findings. Moreover, medical literature supporting a finding of bacterial pneumonia submitted by respondent states: "Occasionally, [a medical examiner] will see a young child with a vague history of some respiratory symptoms over a couple of days, interpreted as being nothing but a cold by the parents. These children are often found to have patchy bronchopneumonia involving all lobes or bronchiolitis." Resp. Ex. MM at 1. K.M.'s examination did not yield any of these findings.

Dr. Vargas was not persuasive in explaining K.M.'s healthy and normal results prior to and leading up to death. K.M. was healthy on examination by her pediatrician on the day of her vaccination; her chest, throat, and ears were clear, and she had been well in the weeks prior with normal hemoglobin. Four days later, upon presentation to the emergency room, her lungs were clear on x-ray and without pulmonary edema; K.M.'s blood tests showed no infection, bacterial or viral. Dr. Vargas's attempt to discredit the blood tests and x-rays taken in the emergency room is not persuasive, particularly in light of the limited neutrophilic findings on the slides. Dr. Perry did not lend credibility to Dr. Vargas's explanation as he did not question the validity of the x-rays when relying on them to opine that K.M. did not have heart failure. The CDC analysis found only parainfluenza virus type 1 and no bacterial or other viral infection, and streptococcus aureus by throat swab was negative. K.M.'s lungs were heavier than normal as were all of her organs on autopsy. Given the significant resuscitation attempts beginning at the doctor's office and the absence of significant histological, laboratory, and imaging evidence supporting bacterial pneumonia, I find the explanation of Drs. Shapiro, Chang, and Waters to be more persuasive. Lifesaving attempts as K.M.'s heart failed likely caused the heaviness of K.M.'s lungs, not bacterial pneumonia.

Lastly, I take seriously the opinion of Dr. Shapiro, placing significant weight on his autopsy findings and his testimony, in addition to the findings of the CDC, the opinion of Dr. Bundock, and the objective evidence in the medical records and the literature filed in this case. Based on their findings and the objective evidence, which is buttressed by the testimony of Drs. Waters and Chang, I find Dr. Shapiro's conclusion to be appropriate and correct: K.M. did not have or die from bacterial pneumonia and sepsis; K.M. died from myocarditis.

b. K.M.'s Myocarditis

1. Eosinophilic and/or Hypersensitivity vs. Lymphocytic and/or Viral Myocarditis

The experts disagreed on what would be required for an eosinophilic or hypersensitivity myocarditis diagnosis.

Dr. Chang opined lymphocytes are typically associated with viral myocarditis and eosinophils with hypersensitivity myocarditis, though he stated the presence of lymphocytes and the absence of eosinophils does not automatically preclude the diagnosis of hypersensitivity

myocarditis. Tr. 130-31; 150. He clarified that hypersensitivity myocarditis is a clinical diagnosis and eosinophilic myocarditis is a diagnosis made based on cell type. More specifically, he opined that given the history and time course in this matter, K.M. experienced a fulminant hypersensitivity myocarditis, in which rapid deterioration occurs within hours to days regardless of whether there is a predominance of eosinophils. *See* Tr. 130; 162-63.

Dr. Chang pointed out that Dr. Perry and Dr. Vargas focused on lymphocytes seen on the heart slides but did not appreciate that there were mononuclear cells that could differentiate into lymphocytes or eosinophils. Further, any infiltration of the heart muscle, whether by mononuclear cells, lymphocytes, or eosinophils, reflects generalized inflammation supporting a clinical diagnosis of myocarditis, even fulminant myocarditis. Tr. 130; 149-50.

According to Dr. Waters, the cell type present in the heart is determinative of the type of myocarditis. Eosinophils are seen in allergic responses, and eosinophilic myocarditis has a population of eosinophils with the possible presence of lymphocytes and neutrophils. Tr. 354-55. She agreed with Dr. Chang's understanding of clinical diagnosis vs. pathological diagnosis, stating, that eosinophils are seen in allergic responses and "[h]ypersensitivity is talking about an allergic reaction and so they're basically pretty much synonymous. The diagnosis generally in clinical terms is considered a hypersensitivity unless they've done a biopsy, because eosinophilic myocarditis is a pathology diagnosis.…So that's why cardiologists will speak more of a hypersensitivity myocarditis." Tr. 373. She also submitted that the number of eosinophils necessary for diagnosis of eosinophilic myocarditis is not well defined; only a few would be needed for diagnosis in an autopsy setting, different than what is required in biopsy. Pet. Ex. 41 at 1-2. Dr. Waters opined that K.M.'s cardiac autopsy slides which included infiltrate of eosinophils, polymorphonuclear leukocytes, plasma cells, and lymphocytes, indicated eosinophilic myocarditis. Pet. Ex. 30 at 3. She also opined that there were more than just a few eosinophils, unlike what Dr. Perry and Dr. Vargas submitted: There were eosinophils scattered throughout the body—in the respiratory tract, liver, esophagus and "in the deltoid muscle where the flu vaccine was given." Tr. 356; 387-89.

Dr. Perry stated hypersensitivity myocarditis would have a predominance of eosinophils. He added that it has a wide range of causes but is most often associated with a drug reaction. Tr. 194. He agreed with Dr. Chang that fulminant myocarditis is acute with rapid evolution within hours or a day or so. However, in Dr. Perry's opinion, fulminant myocarditis is usually viral myocarditis, though he agreed the literature speaks of other causes. Tr. 196-98. Though he never looked at the actual slides in this case, Dr. Perry testified that the images showed mononuclear lymphocytes and no eosinophils, consistent with viral myocarditis. Tr. 225, 262. He later stated he might have seen one or two neutrophils, but at the time, did not look at them. Tr. 225. He then stated that even if he missed a couple of eosinophils it wouldn't change his opinion. Tr. 225-26, 234, 257; 322. In his opinion, a sprinkling of eosinophils would not be sufficient for a hypersensitivity myocarditis, as the literature states a predominance is required. Tr. 227; Tr. 257-58. According to Dr. Perry, the predominance of eosinophils is crucial as shown by *Barton*, in which eosinophilic myocarditis that developed after meningococcal C and hepatitis B vaccinations had a predominance of eosinophils. Tr. 213-14; Pet. Ex. 31. Dr. Perry also pointed to Table 2 of *Barton* showing nine cases of pericarditis, not myocarditis, following influenza vaccinations, noting that pericarditis is a different disease involving the lining, not the muscle, of the heart. Tr.

214, 257; Pet. Ex. 31. Dr. Perry also stated these differences support his opinion that "vaccines are vaccines" is an incorrect statement—each vaccine is made up of different elements. Tr. 254-55.

Dr. Vargas discussed pediatric hypersensitivity myocarditis as histologically showing inflammatory infiltrates consisting predominantly of eosinophils. Tr. 102-03; Resp. Ex. BB at 2; Resp. Ex. I at 2;[123] Pet. Ex. A at 8. "The hallmark [of hypersensitivity myocarditis] is asynchrony between the severity of the infiltrate and little, if any myocyte necrosis, with ultimate resolution of the infiltrate and return to normal cardiac function upon withdrawal of the offending agent." Tr. 106; Resp. Ex. I at 3. According to Dr. Vargas, the proportion of lymphocytes and eosinophils is the determining factor in determining a diagnosis. She opined that small amounts of eosinophils on biopsy in a live patient would be understandable for a diagnosis of eosinophilic myocarditis, but definite amounts of eosinophils would be necessary on autopsy for an eosinophilic myocarditis diagnosis.[124] Dr. Vargas relied on DE A-1 and DE A-2, stating the slides showed "sparse inflammatory infiltrate composed predominantly of lymphocytes with [] areas suspicious for myocyte damage" consistent with lymphocytic myocarditis, typically induced by viral infection. Tr. 107, 117; Resp. Ex. A at 8. Resp. Ex. BB at 2, citing Pet. Ex. 70-3 at 4. She opined that K.M. did not have histologic features of fulminant myocarditis as infiltrate was sparse, though acknowledged that clinically, fulminant myocarditis refers to a myocarditis with a severe course and rapidly progressive process.[125] Tr. 107. She concluded that a diagnosis of eosinophilic myocarditis would be incorrect because eosinophils were only a very small fraction of the inflammatory cells. Resp. Ex. BB at 2.

2. K.M. Died from Eosinophilic and/or Hypersensitivity Myocarditis

While there were lymphocytes found in K.M.'s infiltrate, there were more than a few eosinophils. Tr. 423-24; Resp. Ex. I at 255. There were eosinophils scattered throughout K.M.'s body—in the respiratory tract, liver, esophagus and "in the deltoid muscle where the flu vaccine was given." Tr. 356; 387-89. Dr. Ritter from the CDC found that eosinophils were definitively "impressive in the GI sections!" Pet. Ex. 11. at 19. Though the literature on the number of eosinophils necessary for diagnosis of hypersensitivity myocarditis is unclear, it is clear that both Drs. Vargas and Perry focused solely on cell-type findings in the heart tissue and disregarded the full autopsy findings of eosinophils throughout the organs of the body in concluding there was no hypersensitivity reaction or fulminant myocarditis. Dr. Perry's argument regarding the importance of eosinophil predominance, as found in the cases of eosinophilic myocarditis following meningococcal C or hepatitis B vaccines, is weak due to his own assertion that vaccines are different leaving open the door that eosinophilic and/or hypersensitivity myocarditis following flu vaccination may present differently than eosinophilic and/or hypersensitivity myocarditis following a meningococcal C or hepatitis B vaccination. Dr. Vargas's assertion that there must be a significant number of eosinophils upon autopsy is unfounded, and further, Dr. Vargas herself agreed that fulminant myocarditis, clinically, refers to a myocarditis with a severe course and rapidly progressive process. Tr. 107.

[123] Mirza & Husain, *supra* note 14.
[124] Dr. Vargas did not cite to any literature to support this statement.
[125] Fulminant myocarditis may limit the amount of myocyte damage and infiltrate found if arrhythmia results early on. *See* Pet. Ex. 30 at 4-5 citing *Aslan* and *Seguela; see also,* Tr. 81, 190-91, 204.

Additionally, myocyte necrosis was found on autopsy, a definitive part of a diagnosis for fulminant myocarditis. Tr. 161. The autopsy slides of K.M.'s heart showed multifocal polymorphous white blood cell infiltrate including eosinophils, leukocytes, plasma cells and lymphocytes. The pattern of inflammation was primarily interstitial fibrosis, which is scarring that occurs early in an inflammatory process, within hours to days, and accompanying edema due to inflammatory response. Tr. 355; 371; 373; 412-13; Pet. Ex. 30 at 3. K.M. experienced multi-organ inflammation, anemia, and thrombocytopenia suggestive of a systemic inflammatory process. Pet. Ex. 17 at 3; Pet Ex. 19 at 3. As submitted by Dr. Chang and Dr. Waters, K.M.'s time course and the findings on autopsy indicate that K.M. experienced a fulminant eosinophilic and/or hypersensitivity myocarditis. Pet. Ex. 30 at 3-4; Pet. Ex. 21 at 6; Pet. Ex. 18 at 3-4.

B. Causation and/or Significant Aggravation

a. Petitioner satisfied her burden under *Althen* Prong I/*Loving* Factor IV.

Dr. Shapiro opined that K.M. "died from a hypersensitivity (sic) revved up immune system. She had two very clear instigators of revved up immune system. One, the parainfluenza infection; and two, a vaccination. How that worked in her body to create this hypersensitivity and this myocarditis, I do not know that kind of final physiology…" Shapiro Dep. at 25-26. While Dr. Shapiro did not opine on how the vaccination led to K.M.'s myocarditis, Drs. Waters and Chang provided a theory of cellular immunity leading to myocardial injury.

Dr. Waters described cellular immunity as the process in which antigen-specific cytotoxic T-lymphocytes produce apoptosis in cells containing virus or other targets. T-lymphocytes activate macrophages and natural killer cells which have their own chemical methods to destroy pathogens. "All of these cells produce cytokines which are toxic chemicals." Pet. Ex. 20 at 8. Specifically, Dr. Waters opined that K.M. experienced an anamnestic response to her vaccination, leading to eosinophilic and/or hypersensitivity myocarditis. She explained that when the body has seen an antigen before, such as K.M. receiving flu vaccines annually, memory T cells, rather than naïve T cells, may be able to respond to a lower amount of antigen, and make a wider array of cytokines. Pet. Ex. 21 at 8. During an anamnestic response the body develops cells that attack the previously seen antigen, causing a more robust response on re-exposure, which can be very powerful and very severe. Tr. 366-69. Having a parainfluenza virus type 1 infection at the time of K.M.'s annual flu vaccination likely caused an over stimulation of the immune response leading to an excess of cytokines magnifying their toxic effects. Tr. 452; Pet. Ex. 20 at 8. Dr. Waters opined that the side effects of vaccines can follow the pattern of the complications of a natural infection of influenza causing myocarditis. *Id.* at 11; *See* Pet. Ex. 25.[126]

Supporting Dr. Waters's theory, Dr. Chang similarly opined that the vaccine caused a hypersensitive immune response leading to myocardial injury. He cited *Thanjan*, a case report involving post-vaccination acute myopericarditis in a 17-year-old who received DTaP, meningococcal conjugate, and hepatitis A vaccines. Pet. Ex. 17 at 2n.1; *see* Pet. Ex. 18.[127] The proposed mechanism of myocardial injury in *Thanjan* was hypersensitivity reaction, as in this

[126] Institute of Medicine, *supra* note 70.
[127] Thanjan et al., *supra* note 57.

matter. The pathogenesis of myocardial injury was a maladaptive immune response involving CD3+ T-cell infiltrate with prominent degranulating eosinophils. *See* Pet. Ex. 18 at 3. While the case report in *Thanjan* is not completely identical to K.M.'s situation, the biological mechanism applies in the same manner.

The theories proposed by Drs. Chang and Waters's, combined with Dr. Shapiro's autopsy findings, provide a persuasive theory for how K.M.'s December 2, 2011 flu vaccine resulted in eosinophilic and/or hypersensitivity myocarditis. Based on testing conducted in the emergency room, by Dr. Shapiro, and at the CDC, an underlying parainfluenza virus type 1 existed at the time the flu vaccine was administered. As submitted by Drs. Chang and Waters, the flu vaccine, with its intended effect to induce proinflammatory cytokines sufficient to activate the immune system into producing antibodies against an influenza infection, acted as a subsequent immune challenge to an already activated immune system. The flu vaccine increased cytokine upregulation and caused a hypersensitivity response with eosinophil production. When eosinophils respond to allergic reactions, they can misdirect to normal tissue and damage organs such as the lungs, heart, kidneys, and brain. Here, eosinophils were found throughout K.M.'s body. K.M.'s autopsy showed multi-organ inflammation with findings of anemia and thrombocytopenia, suggestive of a systemic inflammatory process. The flu vaccine overstimulated her immune system resulting in eosinophils infiltrating her heart, causing eosinophilic and/or hypersensitivity myocarditis.

Petitioner's experts also successfully explained how eosinophilic and/or hypersensitivity myocarditis led to K.M.'s death. As explained by Dr. Waters, eosinophils orchestrate a robust immune inflammatory response that destroys invading microbes, foreign tissue, and malignant cells. They contain granules that, when released, induce the production of toxic proteins and cytokines that cause tissue damages, including necrosis. When eosinophils infiltrate the heart, three stages of eosinophilic myocarditis can occur: acute necrotic, thrombotic, and fibrotic. Without early diagnosis, the acute necrotic stage can be rapidly fatal; patients can present with heart failure or arrhythmia. The fibrotic stage is irreversible scarring within the heart with clinical findings of restrictive cardiomyopathy. Histology at this stage shows fibrosis with few eosinophils or other inflammatory cells. Myocarditis also affects the regulation of heartbeats, causing dysrhythmia with symptoms of fatigue and other abnormalities. Tr. 358. There was no dispute among any of the experts that myocarditis, regardless of type, causes heart muscle cell damage which can cause heart failure. The experts acknowledged that an arrhythmia can result at any point due to scarring from inflammation. *See* Tr. 81, 190-91, 204. When there is fulminant myocarditis, or myocarditis that is rapidly progressive and severe, there may not be significant necrosis if dysrhythmia occurs early on and causes immediate death. Given the time course and the myocyte necrosis found on autopsy, K.M. experienced fulminant myocarditis which resulted in her death. Tr. 161.

Accordingly, I find that petitioner's experts have proffered a sound, reliable theory that an already stimulated and reactive immune system responding to a viral infection would be further stimulated by the receipt of a flu vaccine intended to elicit an immune response. The two combined would be capable of orchestrating a robust immune response releasing eosinophils throughout the body. This process of eosinophil production occurred in K.M.'s otherwise healthy body and damaged her organs and heart, causing an arrythmia and death. Pet. Ex. 20 at 8.

Petitioner has satisfied *Althen* Prong I/*Loving* Factor IV.

b. Petitioner satisfied her burden under *Althen* Prong II/*Loving* Factor V.

Petitioner's experts presented a logical sequence of cause and effect showing that the December 2, 2012 vaccination was a substantial factor in K.M.'s death.

This case resembles *Shyface v. Sec'y of Health & Human Services*, in which a baby was vaccinated with whole-cell DPT at the time he was beginning an *E. coli* infection. Both the DPT and the *E. coli* infection could and did cause fever, which rose to 110 degrees, resulting in the child's death four days later. 165 F.3d. at 1345. Respondent defended the case and argued that the *E. coli* infection was the cause of the baby's fever and death. Testimony from petitioner's treating physician was that both the vaccine and the infection were equally responsible for his fever and death. The Federal Circuit held that each of the two factors, the vaccine and the infection, was a substantial factor in causing the baby's very high fever and death and but for the vaccination, the baby would not have had the high fever and would not have died. The Federal Circuit ruled in favor of petitioner though petitioner did not prove that DPT vaccine was the only or predominant cause of death. *Id*. at 1353.

Here, the facts and expert opinions in this matter demonstrate that K.M., but-for the vaccination, would not have died. The administration of a flu vaccine to K.M.'s already "revved-up" body fighting a parainfluenza virus resulted in cytotoxic levels of cytokines and eosinophils circulating throughout her body. This triggered a process, leading to myocarditis and death, that neither the parainfluenza virus nor the vaccine could have triggered alone. Even though K.M. experienced a concomitant parainfluenza virus type 1 infection, the vaccine was a substantial factor in causing her death.

On the day of vaccination, K.M. had a normal physical examination, with ears clear, no rhinorrhea, no mouth lesions, no tonsillar hypertrophy, neck supple with no thyromegaly and no regional adenopathy of the lymph nodes. There was no heart murmur, her lungs were clear, her abdomen soft, she had full range of motion of all joints, and there no swelling and no neurological symptoms. She had no rashes, hemoglobin was normal, urinalysis was normal, and hearing and vision were normal. Chest x-rays in the emergency room four days later were normal with no fluid in the lungs and white blood count was normal with no elevation indicative of viral or bacterial infection. Postmortem cultures of the lung, spinal fluid and blood were negative for bacteria and negative for influenza A and B, enterovirus and RSV. Immunohistochemistry for enterovirus on the heart was negative.

Petitioner's description of K.M. in the days that followed her vaccination support K.M.'s experiencing a hypersensitivity reaction which began with a headache controlled by Tylenol initially but kept returning, sleepiness, nausea and fever of 102.3 uncontrolled by Tylenol. She then developed body aches, continued to vomit and complain of headache and body aches while Tylenol and ibuprofen were given as directed by the pediatrician on call. On December 5, 2011, K.M. still had a fever, was lethargic, complained she did not know where she was and slept most of the day. The night of December 5, 2011 into the morning of December 6, 2011, K.M. kept waking, crying that her body and head still hurt "really bad" and continued to throw up. She cried most of the night, could not get comfortable and was in pain. By the next morning she was cold,

her skin on her legs and arm "blotchy purple," her lips purple, she struggled to breath and ultimately, stopped breathing. Pet. Ex. 44 at 2-3. Consistent with K.M.'s presentation, clinical signs of eosinophilic myocarditis include fever, chills, malaise, weight loss, acute coronary syndrome-like features, heart failure, tachy-or brady-type arrhythmias, and sudden death. Pet. Ex. 37 at 3.

Dr. Shapiro stated, "[M]y thoughts are this kid had a revved up immune system, possibly from the Para influenza, then got the vaccination, designed to give an immune response, and she developed some type of systemic hypersensitivity resulting in the myocarditis and other findings." Pet. Ex. 11 at 17. Dr. Waters added that the widespread findings of mixed inflammatory response with lymphocytes and eosinophils was an indicator of allergy or IgE mediated hypersensitivity response. Pet. Ex. 46 at 2. Further, K.M.'s receipt of flu vaccines every year created memory T cells capable of responding to lower amounts of peptide antigen, making a wider array of cytokines, that rapidly became cytolytic. Pet. Ex. 21 at 8. Dr. Chang opined that K.M. experienced a hypersensitivity myocarditis based on history and the temporal relationship of an inciting agent in the absence of other significant factors. Tr. 148.

Until the hearing, respondent argued that the parainfluenza virus was the sole cause of viral myocarditis resulting in arrythmia and K.M.'s death. However, during and following the hearing, Dr. Vargas abandoned myocarditis, opining that parainfluenza virus type 1 resulted in a fatal bacterial pneumonia with sepsis causing death. As discussed above, I find that K.M. did not suffer from a fatal bacterial pneumonia that caused sepsis and death. Moreover, Dr. Perry and Dr. Vargas's initial opinions did not persuasively explain how the only cause of K.M.'s myocarditis was from an unremarkable and asymptomatic parainfluenza virus type 1 infection. Neither of respondent's experts submitted any literature that supported parainfluenza virus type 1 as a cause of myocarditis. Petitioner's experts noted that the literature Dr. Vargas did rely upon involved adult parainfluenza virus type 3 and myocarditis, not pediatric parainfluenza virus type 1. Dr. Chang further noted that K.M. did not have any diseases caused by parainfluenza type 1 virus at the time of vaccination, nor is parainfluenza type 1 associated with cardiac disease. Therefore, I do not find that the respondent has persuasively shown that K.M.'s parainfluenza virus type 1 infection was the sole factor in bringing about her death.

In accordance with *Shyface*, I find that both the parainfluenza virus type 1 infection and vaccination played a role in K.M.'s death, with the December 2, 2011 vaccination being a substantial factor. But for the influenza vaccine, K.M. would not have died.

Petitioner has satisfied *Althen* Prong II and *Loving* Prong V.

c. Petitioner satisfied her burden under *Althen* Prong III/*Loving* Factor VI.

Though timing was barely addressed in this case, based on the evidence presented, I find that K.M.'s time course is appropriate.

Drs. Shapiro, Chang and Waters opined that K.M.'s onset of symptoms within 24 hours that progressed and culminated in her death fewer than four days after the vaccination was appropriate for a systemic response with or without the accompanying parainfluenza virus type 1.

Dr. Perry agreed that fulminant myocarditis following a drug, though he argued vaccines are not a drug, is rapid after exposure. Dr. Vargas did not address timing at all other than to suggest that K.M. suffered from a chronic upper respiratory infection that was ongoing for at least a week if not as long as a month.

Generally, responses to a new antigen occur within five to ten days. Where there are memory T cells, due to prior exposure, the response is a wider array of cytokines, that rapidly become cytolytic and become home to either lymphoid or non-lymphoid compartments. T cells have a 48 to 72-hour lag time before they become active in all those areas. They can also proliferate as rapidly as every two hours. Pet. Ex. 21 at 8. With an anamnestic response, the reaction is quicker and more powerful. Pet. Ex. 30 at 5; Pet. Ex. 34-39.

Accepting all of the experts posturing on timing, I find *Bragg v. Sec'y of Health & Human Services* persuasive and applicable under the given circumstances. In *Bragg*, the vaccinee "felt ill 30 minutes after receiving the flu vaccination. He never felt any better but continued to get worse until he died." 2012 WL 404773, at *26 (Fed. Cl. Spec. Mstr. Jan. 18, 2012). The special master concluded:

> The timing is compelling in this case….When someone becomes ill with a vaccine injury and worsens day by day until he dies, a reasonable conclusion is that the immunologic challenge caused the illness….In the instant action, the timing of decedent's onset of his mortal illness is consistent with systemic inflammation response syndrome, the response being to flu vaccination.

Id. at *26-27. Notably, the vaccinee's symptoms began shortly after vaccination and continued to progress until his death five days post-vaccination. *Id*. at *1.

Here, K.M. developed a headache the day after her vaccination with fever of 102, vomiting, body aches and ultimately dyspnea expiring less than four days after her vaccination. The timing of K.M.'s clinical course was similar with progressive deterioration beginning the day after the vaccination and culminating in death three days later. Like the special master in *Bragg*, I find the timing of K.M.'s receipt of the influenza vaccine and subsequent deterioration quite compelling.

Petitioner has satisfied *Althen* prong III/*Loving* factor VI.

d. *Loving* Factor I: K.M.'s Health Prior to Vaccination

K.M. had no symptomatic or chronic illness prior to her influenza vaccine and was determined to be a well child. On the day of her vaccination, she did not present with any upper respiratory symptoms and no respiratory findings were made on examination. However, the testing demonstrated that she had an asymptomatic parainfluenza virus type 1 infection. All other viruses tested for were negative as was testing for bacterial infection.

e. *Loving* Factor II: K.M.'s Deterioration

K.M. deteriorated rapidly following her December 2, 2011 flu vaccine. One need not look further than petitioner's affidavit (Section III(B)(a)) which details the days following K.M.'s influenza vaccine and how her health deteriorated beginning one day post-vaccination until her death the morning of December 6, 2011.

f. *Loving* Factor III: Significant Aggravation vs. Natural Progressive Disease

K.M. did not die solely due to a natural progressive disease. Dr. Perry opined K.M. died from parainfluenza virus type 1 resulting in viral myocarditis. Dr. Vargas opined K.M. died of a fatal bacterial pneumonia and sepsis secondary to parainfluenza virus type 1. Dr. Perry then agreed with Dr. Vargas but maintained myocarditis as the mechanism of death. For the reasons more specifically set forth above (Section IV(A)(a)), K.M. did not suffer from a fatal bacterial pneumonia secondary to an asymptomatic parainfluenza virus type 1. The eosinophils, inflammation and edema found throughout her body and brain support an acute systemic response, not a naturally progressive disease.

C. Burden Shifting: Alternative Cause

a. Respondent Failed to Prove an Alternative Cause of Injury

Because petitioner has established a prima facie case of causation under *Althen* / *Loving*, she is entitled to compensation unless respondent can show by a preponderance of the evidence that K.M.'s death was in fact caused by a factor unrelated to the vaccines. *Deribeaux*, 717 F.3d at 1367; *see* § 13(a)(1)(B). To meet this standard, respondent must "present sufficient evidence to prove that the alternative factor was the sole substantial factor in bringing about the injury." *Deribeaux*, 717 F.3d at 1367. The Vaccine Act limits the scope of unrelated factors by excluding any "idiopathic, unexplained, unknown, hypothetical or undocumentable cause, factor, injury, illness or condition." § 13(a)(2)(A). "In other words, alternative causes that are 'idiopathic, unexplained, unknown, hypothetical or undocumentable' cannot overcome a petitioner's prima facie case." *Doe*, 601 F.3d at 1357 (quoting § 13(a)(2)(A)).

Dr. Vargas stood alone in her theory that a fatal bacterial pneumonia and sepsis caused K.M.'s death.[128] With due deference to Dr. Vargas's expertise in lung pathology, her conclusion that K.M. suffered a fatal pneumonia and sepsis was based on her interpretation of focal findings on a random slide largely uncorroborated by any other physician in this case or the "other evidence" found on autopsy.

In Dr. Vargas's opinion, all the doctors in this case were wrong, and there was no allergic response. Tr. 311; 525-526. She opined that Dr. Chang is not a pathologist and failed to see "all the pieces of the puzzle in the right way." Tr. 527. She submitted that K.M. would have died even if she didn't receive the flu vaccine. Tr. 555-56. She stated the immune response to the parainfluenza virus was substantial with significant inflammation throughout respiratory tract.

[128] Dr. Perry somewhat aligned his opinion with Dr. Vargas following her testimony, opining that K.M. likely had bacterial pneumonia.

> "And that's just something that has to do with luck if you happen to aspirate it and you can't clear it because of your viral infection. I don't see it being related to the virus or – sorry, to the vaccination in any way. I see it being related to bad luck in the setting of a viral infection. That's the way I see it."

Tr. 556-57.

I found Dr. Vargas's pointed attention on K.M.'s heavy lung weight as proof of bacterial pneumonia unpersuasive. She conceded the lungs were her only interest because, "…if you want to make a diagnosis of pneumonia, it's good to make sure the lung weight is increased before you do so, so that you can make sure that all the parameters are aligned behind the diagnosis that you want to make." Tr. 52-55. Pet. Ex. 10 at ECF 7; Resp. Ex. E. From that point onward, Dr. Vargas focused all her testimony only on the evidence she deemed supportive of her opinion, a deadly bacterial pneumonia and disregarded everything else. In doing so, Dr. Vargas boldly stated that Drs. Waters, Chang, Shapiro, Dr. Bundock and the scientists at the CDC, none of whom saw a deadly pneumonia in this case, were all wrong. Not only did Dr. Vargas reject the aforementioned scientists' opinions in this matter, she also constructively disagreed with Dr. Perry's assessment, who, unlike Dr. Vargas, is a clinician regularly treating pediatric cardiology patients. Her final opinion in this matter was decidedly limited and fixed on K.M.'s lungs and her interpretation of K.M.'s lungs. Dr. Vargas seemingly chose to disregard anything unsupportive or contrary to her opinion. For example, Dr. Vargas opined that K.M. could not have been healthy, therefore her physician missed symptoms; the x-rays in the emergency room being clear without pulmonary edema was because pneumonia lags behind, the equipment was not sufficient, or the x-ray technician lacked skill; the blood work taken at the emergency room also having normal results, was because the test was not reliable. Tr. 63; 70-71; 95-96; 479-82. Considering all the above, I do not find that K.M. had bacterial pneumonia and sepsis as the evidence does not support such a finding.

Dr. Perry's opinions were no more persuasive than Dr. Vargas's opinion. Dr. Perry opined that respiratory and cardiac inflammation from a viral etiology are fairly common clinical associations, with parainfluenza virus type 1 "being an active infectious agent responsible for this child's demise." Resp. Ex. P at 3-4. He opined K.M.'s myocarditis was "clearly lymphocytic, as recognized as the classic finding in viral myocardial inflammation" and not hypersensitivity reaction which involves eosinophilic infiltrate. *Id*.; *see* Resp. Ex. R;[129] Resp. Ex. S.[130] However Dr. Perry's argument regarding the importance of eosinophil predominance for hypersensitivity reaction is weak as the literature is unclear on how many eosinophils need to be present and the literature he cited was not on point. He failed to address the eosinophils scattered throughout K.M.'s body—in the respiratory tract, liver, esophagus, and in the deltoid muscle where the flu vaccine was given. Dr. Perry never reviewed the slides in this matter yet opined that even if he had missed eosinophils, he would not change his opinion. Further, even though literature speaks of other causes, which he acknowledged, Dr. Perry opined that fulminant myocarditis is usually viral myocarditis; thus, K.M.'s fulminant myocarditis must have been lymphocytic myocarditis. *Id*.

[129] Vignola et al., *supra* note 103.
[130] Shauer et al., *supra* note 104.

Dr. Perry could not state with certainty whether K.M. suffered respiratory arrest with subsequent cardiac decompensation and ventricular tachyarrhythmia, a cardiac ventricular arrhythmia coinciding with respiratory illness, or myocarditis causing complete atrioventricular block; however, he still concluded that the viral infection was the etiology. Resp. Ex. P at 4. "Her death was clearly most likely due to Parainfluenza infection and not from any idiosyncratic or other reaction to an influenza vaccine." Resp. Ex. P at 4. Dr. Perry maintained that K.M. died from lymphocytic myocarditis, even after Dr. Vargas referred to myocarditis in this case as a "red herring" and that the cause of death was fatal bacterial pneumonia and sepsis. Tr. 188-189; 221. Dr. Perry's opinion did not support Dr. Vargas's and Dr. Vargas's final opinion completely rejected Dr. Perry's. As detailed more thoroughly above, I do not find that K.M. had or died of lymphocytic myocarditis, but rather from hypersensitivity myocarditis.

Respondent has failed to satisfy his burden in showing an alternative cause. I do not find that K.M. developed a deadly bacterial pneumonia or lymphocytic myocarditis over the four days following her flu vaccine resulting in her death.

VII. CONCLUSION

Upon careful evaluation of all the evidence submitted in this matter—the medical records and tests, the testimony of petitioners, and the experts' opinions and medical literature—I find that petitioner has shown that she is entitled to compensation under the Vaccine Act. Petitioner has put forth preponderant evidence that the influenza vaccine K.M. received on December 2, 2011 was a substantial factor in her death and respondent has failed to rebut that showing. Accordingly, this matter shall proceed to damages.

IT IS SO ORDERED.

s/ Mindy Michaels Roth
Mindy Michaels Roth
Special Master